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LOGINID:SSSPTA1612RXD
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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS 10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS 11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
NEWS 13	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
NEWS 18	Oct 22	DGENE GETSIM has been improved
NEWS 19	Oct 29	AAASD no longer available
NEWS 20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 22	Nov 29	COPPERLIT now available on STN
NEWS 23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 24	Nov 30	Files VETU and VETB to have open access
NEWS 25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26	Dec 10	DGENE BLAST Homology Search

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:06:27 ON 13 DEC 2001

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'REGISTRY' ENTERED AT 15:06:35 ON 13 DEC 2001

STRUCTURE FILE UPDATES: 11 DEC 2001 HIGHEST RN 374745-93-4
DICTIONARY FILE UPDATES: 11 DEC 2001 HIGHEST RN 374745-93-4

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 9806952.str

L1 STRUCTURE UPLOADED

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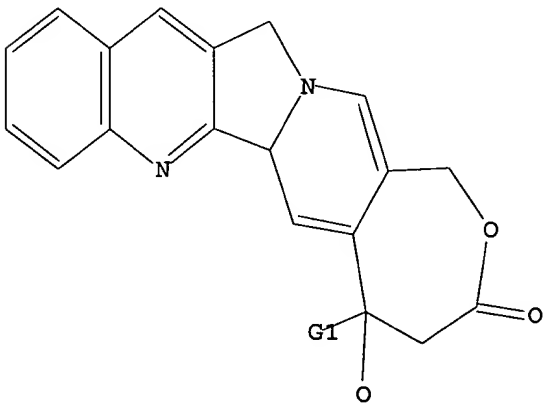
L1 HAS NO ANSWERS
L1 STR



G1 Ak,H

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -      8 TO ITERATE

100.0% PROCESSED       8 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            8 TO      329
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> s l1 ful
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FULL SCREEN SEARCH COMPLETED -    354 TO ITERATE

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SEARCH TIME: 00.00.01

L3             0 SEA SSS FUL L1

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Uploading 9806952.str

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L4 HAS NO ANSWERS
L4                STR
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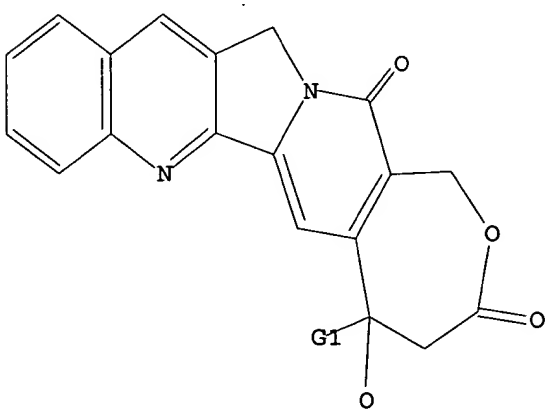

G1 Ak,H

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 8 TO ITERATE

100.0% PROCESSED 8 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8 TO 329
PROJECTED ANSWERS: 5 TO 234

L5 5 SEA SSS SAM L4

=> s l4 ful
FULL SEARCH INITIATED 15:09:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 354 TO ITERATE

100.0% PROCESSED 354 ITERATIONS 197 ANSWERS
SEARCH TIME: 00.00.01

L6 197 SEA SSS FUL L4

=> file uspatfull
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 268.05 268.20

FILE 'USPATFULL' ENTERED AT 15:09:37 ON 13 DEC 2001
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 13 Dec 2001 (20011213/PD)
FILE LAST UPDATED: 13 Dec 2001 (20011213/ED)
HIGHEST GRANTED PATENT NUMBER: US6249914
HIGHEST APPLICATION PUBLICATION NUMBER: US2001051434
CA INDEXING IS CURRENT THROUGH 13 Dec 2001 (20011213/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Dec 2001 (20011213/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2001
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2001

>>> Page images are available for patents from 1/1/1998. Patents <<<
>>> and applications are typically loaded on the day of publication.<<<
>>> Page images are available for display by the following day. <<<
>>> Image data for the /FA field are available the following update.<<<

>>> Complete CA file indexing for chemical patents (or equivalents) <<<
>>> is included in file records. A thesaurus is available for the <<<
>>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<
>>> fields. This thesaurus includes catchword terms from the <<<
>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
>>> available for the WIPO International Patent Classification <<<
>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<
>>> the /IC5 and /IC fields include the corresponding catchword <<<
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

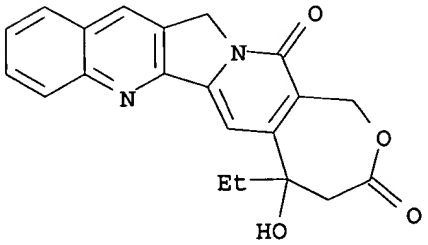
=> s l6
L7 5 L6

=> d abs bib hitstr 1-5

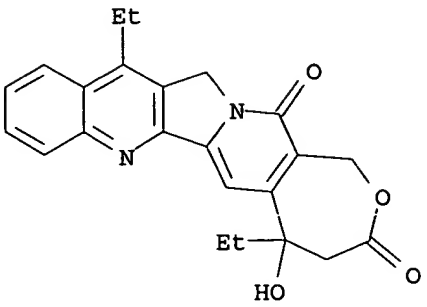
L7 ANSWER 1 OF 5 USPATFULL
AB A compound of the formula ##STR1##

wherein the substituents are as defined in the specification and a method of inhibiting tumors.

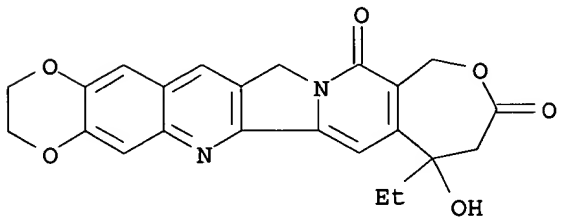
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:197032 USPATFULL
TI Analogues of camptothecin, preparation procedures, their application as medicines and the pharmaceutical compositions comprising them
IN Bigg, Dennis, Gif-sur-Yvette, France
Lavergne, Olivier, Massy, France
Pla Rodas, Francesc, Santa Coloma de Farners, Spain
Pommier, Jacques, Colombes, France
Ulibarri, Gerard, Bures-sur-Yvette, France
PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S.), France (non-U.S. corporation)
PI US 6313135 B1 20011106
AI US 1999-325913 19990604 (9)
RLI Continuation of Ser. No. US 1997-973561, filed on 2 Dec 1997, now patented, Pat. No. US 5981542
PRAI GB 1995-12670 19950621
US 1996-8610476 19960304
WO 1996-FR980 19960621
DT Utility
FS GRANTED
EXNAM Primary Examiner: Kifle, Bruck
LREP Bierman, Muserlian and Lucas
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2424
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **186668-40-6P 186668-44-0P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-40-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



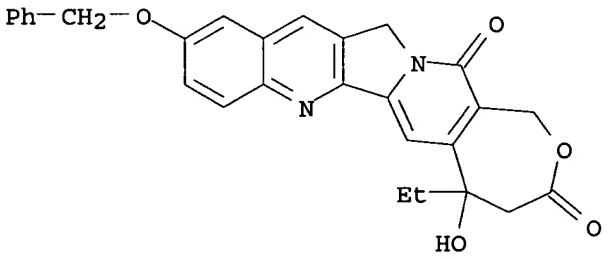
RN 186668-44-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



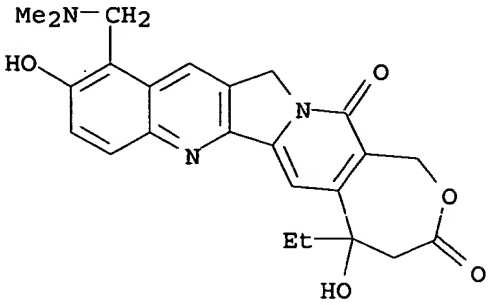
IT **186668-59-7P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-59-7 USPATFULL
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)



IT **186668-63-3P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-63-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)



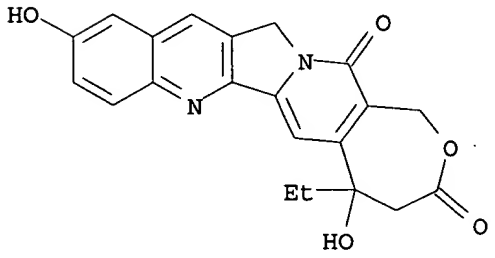
IT **186668-66-6P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-66-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



IT **186668-65-5P 186668-67-7P 186668-68-8P**
186668-69-9P 186668-70-2P 186668-71-3P
186668-72-4P 186668-73-5P 186668-74-6P
186668-75-7P 186668-77-9P 186668-79-1P
186668-81-5P 186668-83-7P 186668-90-6P
186668-94-0P 186669-03-4P 186669-04-5P
186669-06-7P 186669-07-8P 186669-08-9P
186669-09-0P 186669-10-3P 186669-12-5P
186669-13-6P 186669-14-7P 186669-16-9P
186669-18-1P 186669-19-2P 186669-20-5P
(prepn. of camptothecin analogs as antitumor agents)

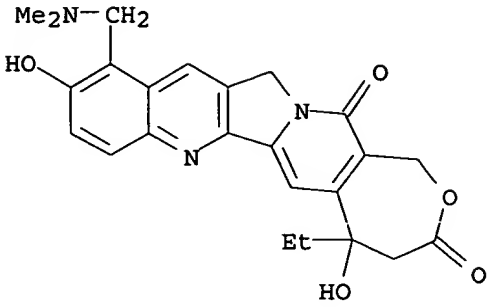
RN 186668-65-5 USPATFULL

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



RN 186668-67-7 USPATFULL

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 186668-68-8 USPATFULL
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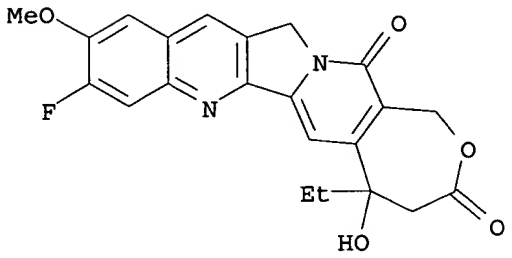

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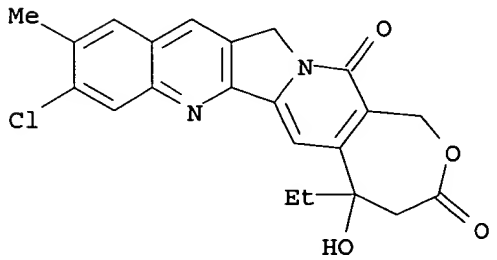
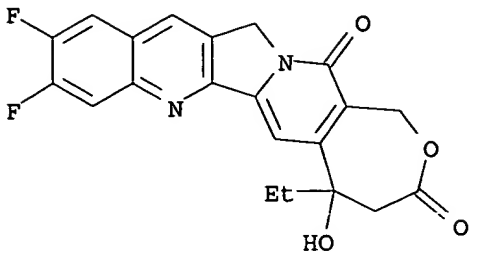
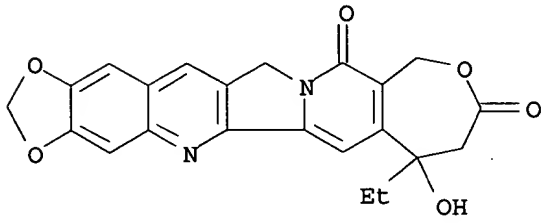


RN 186668-70-2 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-71-3 USPATFULL
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-72-4 USPATFULL
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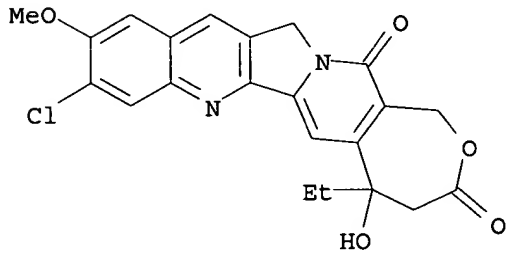

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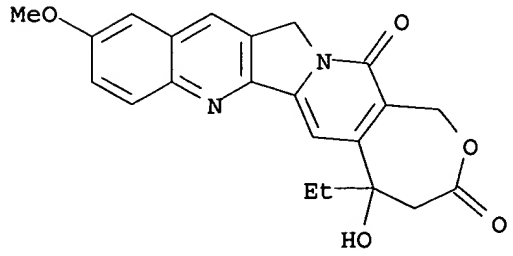

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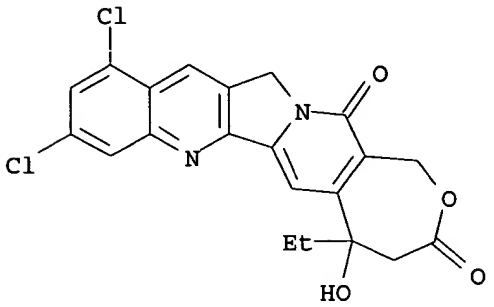

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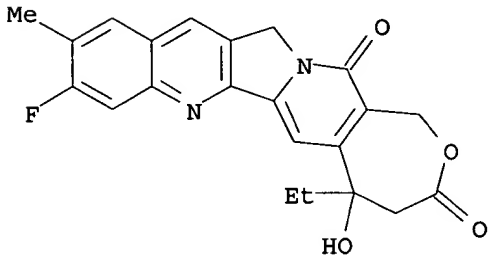

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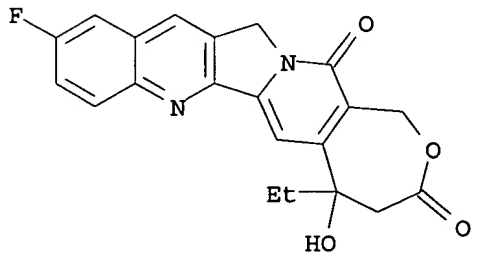

RN 186668-79-1 USPATFULL
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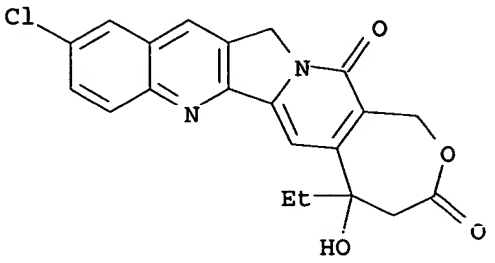

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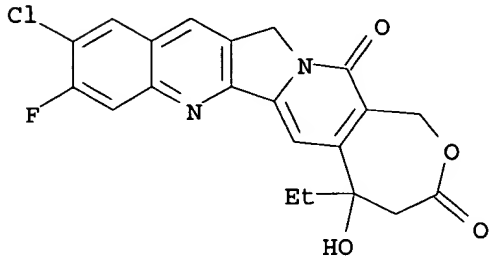
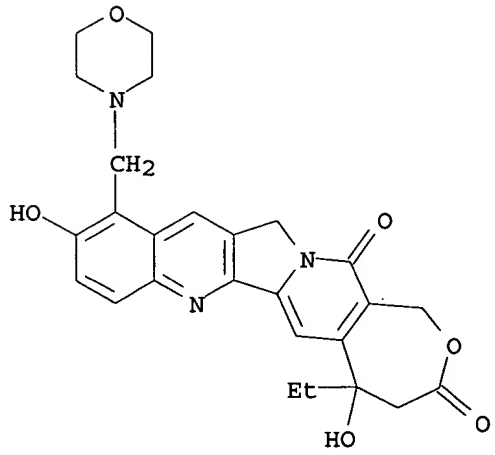
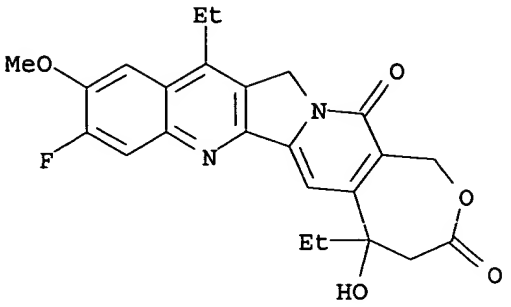


RN 186668-83-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-11-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



RN 186668-90-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



RN 186668-94-0 USPATFULL
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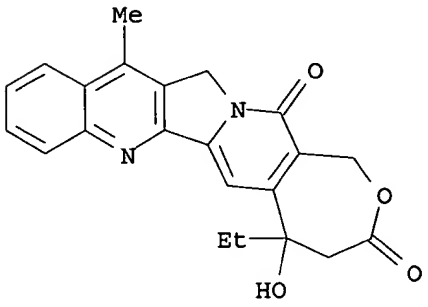
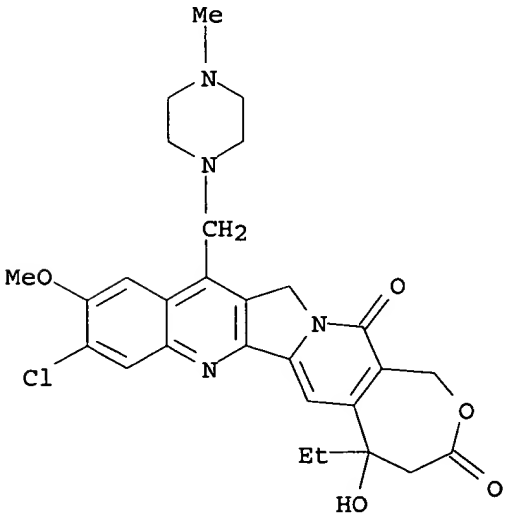
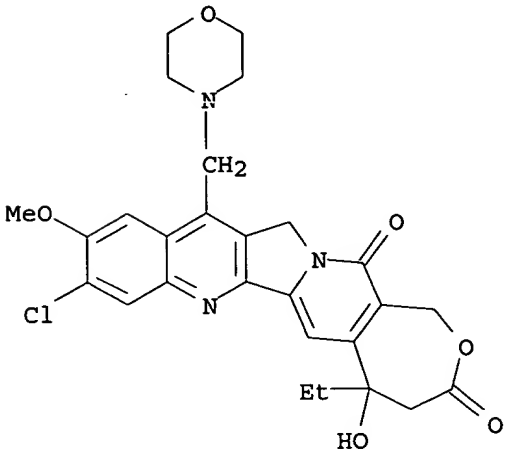


RN 186669-03-4 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

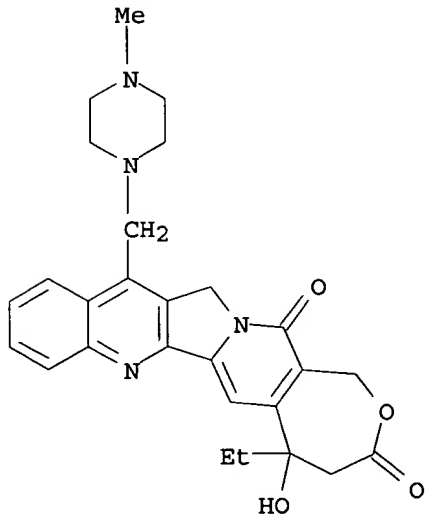


RN 186669-04-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

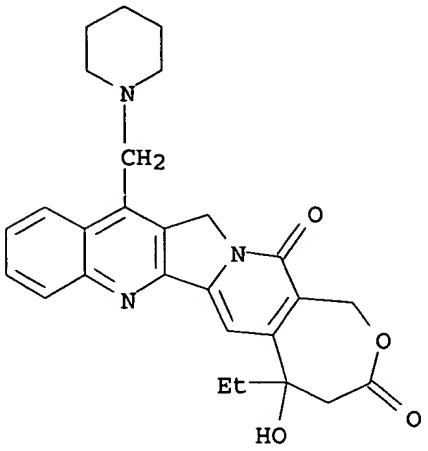
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



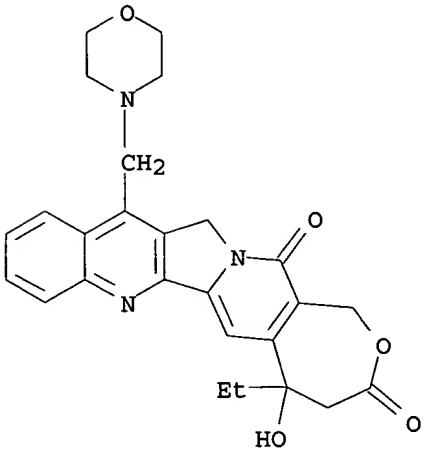
RN 186669-06-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



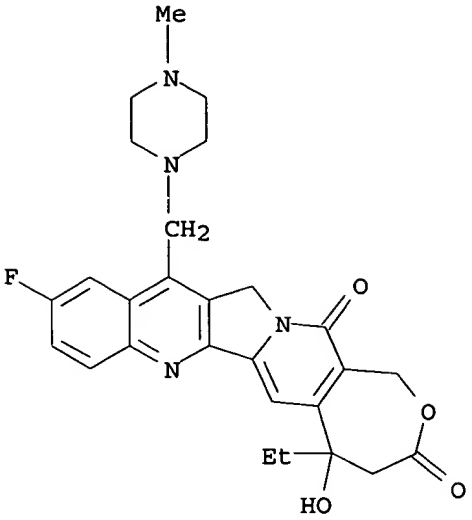
RN 186669-07-8 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



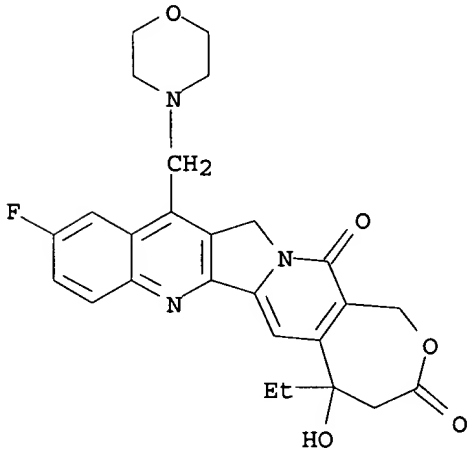
RN 186669-08-9 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



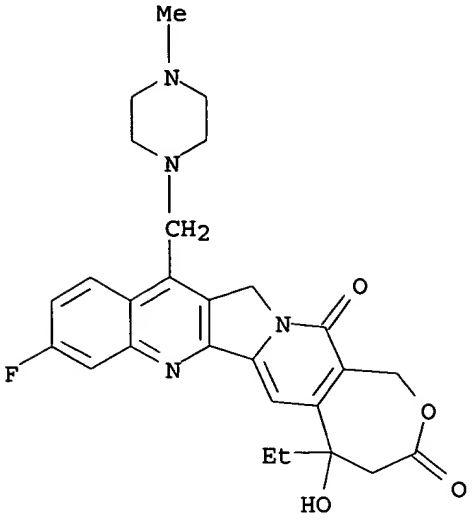
RN 186669-09-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



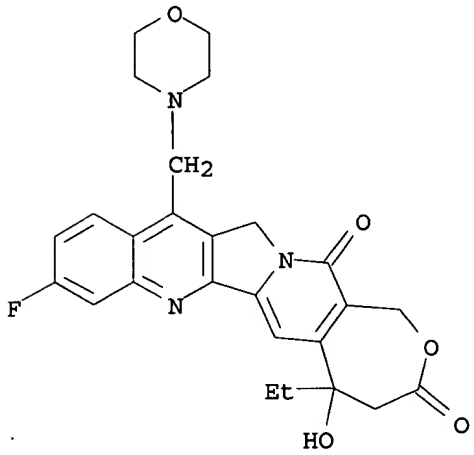
RN 186669-10-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



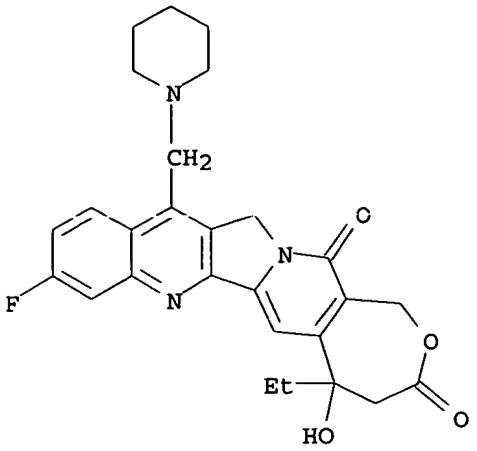
RN 186669-12-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



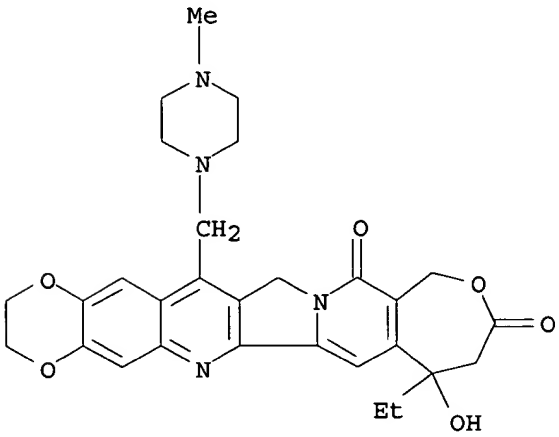
RN 186669-13-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)-
(9CI) (CA INDEX NAME)



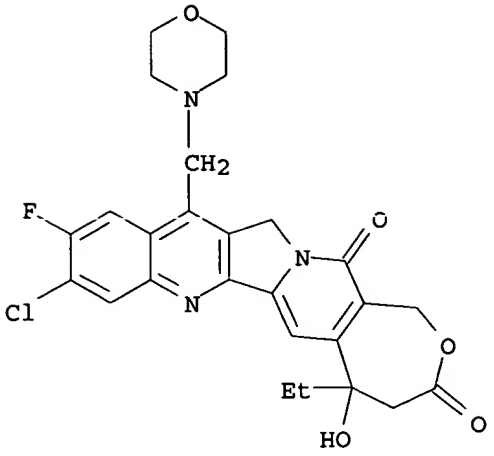
RN 186669-14-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)-
(9CI) (CA INDEX NAME)



RN 186669-16-9 USPATFULL
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy-16-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

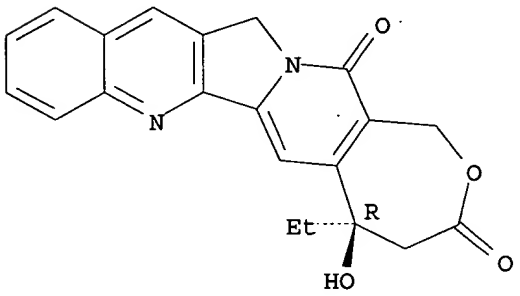


RN 186669-18-1 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



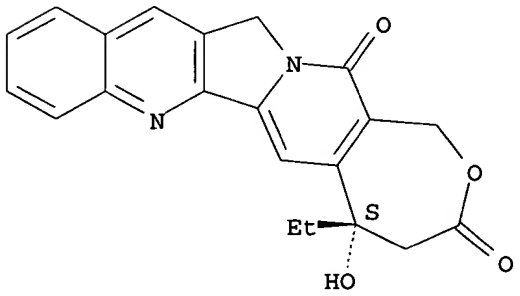
RN 186669-19-2 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186669-20-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5S)- (9CI) (CA INDEX NAME)

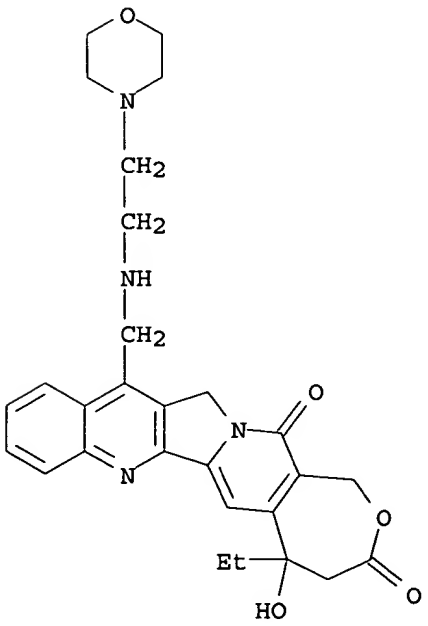
Absolute stereochemistry.



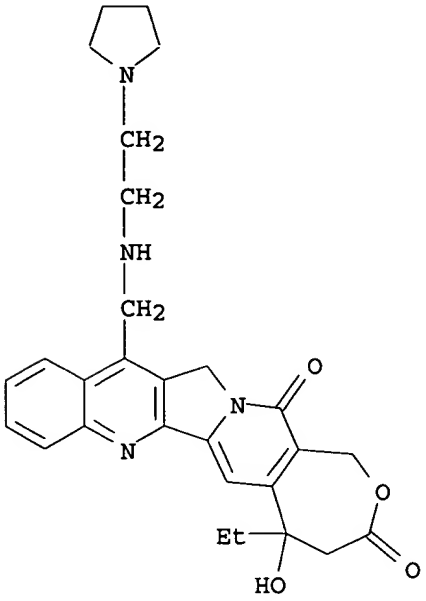
L7 ANSWER 2 OF 5 USPATFULL
AB Camptothecin and homocamptothecin analogs and derivatives are provided

incorporating alkylamine and polyalkylamine moieties.

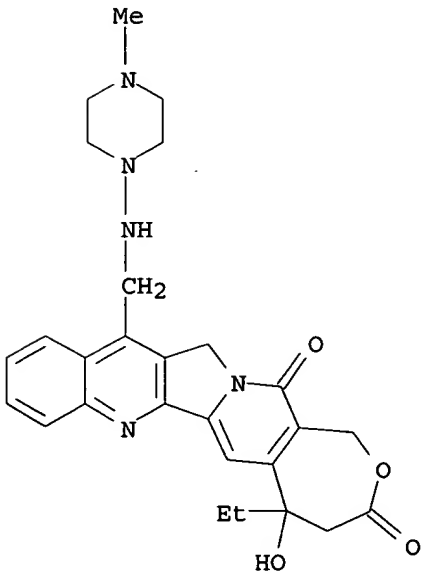
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:158493 USPATFULL
TI Water-soluble derivatives of camptothecin/homocamptothecin
IN Burke, Thomas G., Lexington, KY, United States
Demir, Ayhan S., Neunkirchen, Turkey
Tanyeli, Cihangir, Ankara, Turkey
Chavan, Ashok J., Lexington, KY, United States
Wang, Tie-Lin, San Diego, CA, United States
Pommier, Yves, Bethesda, MD, United States
PA University of Kentucky Research Foundation, Lexington, KY, United States (U.S. corporation)
PI US 6291676 B1 20010918
AI US 2000-517210 20000302 (9)
PRAI US 1999-122621 19990303 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Kifle, Bruck
LREP King and Schikli, PLLC
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 2611
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **360071-33-6P 360071-34-7P 360071-35-8P**
360071-36-9P 360071-37-0P 360071-38-1P
360071-39-2P 360071-40-5P 360071-41-6P
360071-42-7P
(prepn. of water-sol. camptothecin/homocamptothecin derivs.)
RN 360071-33-6 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[[[2-(4-morpholinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 360071-34-7 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[[[2-(1-pyrrolidinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)

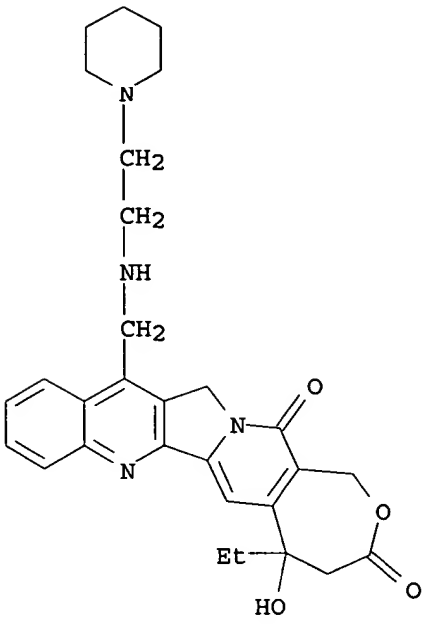


RN 360071-35-8 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[[(4-methyl-1-piperazinyl)amino]methyl]- (9CI) (CA INDEX NAME)

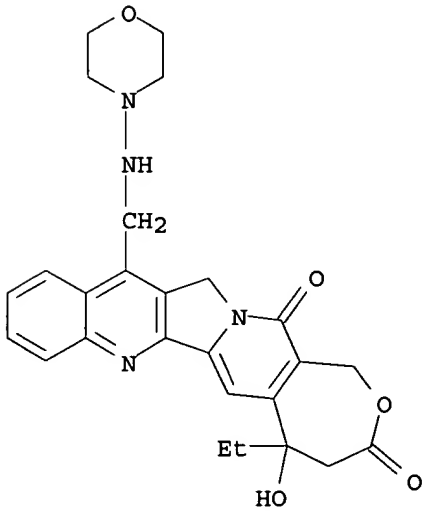


RN 360071-36-9 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione,

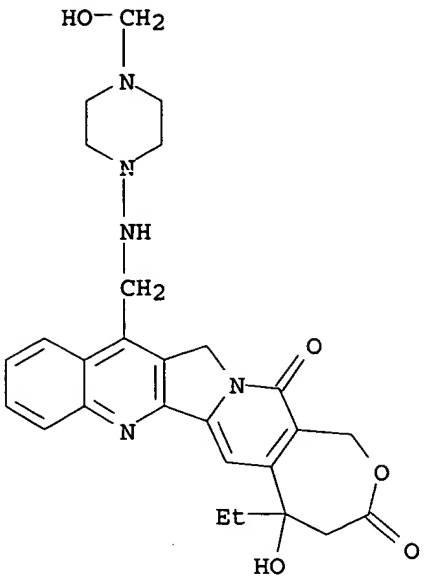
5-ethyl-4,5-dihydro-5-hydroxy-12-[[[2-(1-piperidinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)



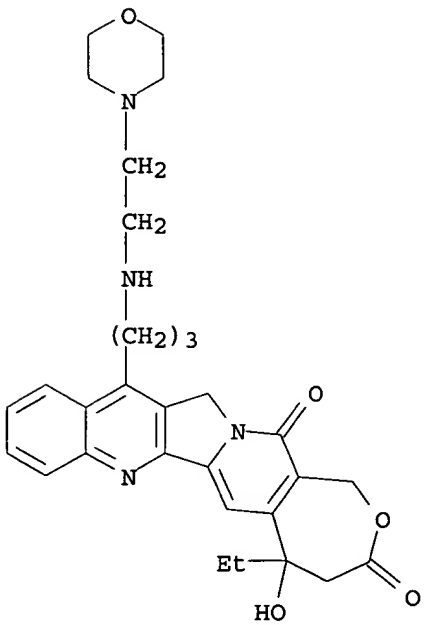
RN 360071-37-0 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[(4-morpholinylamino)methyl]- (9CI) (CA INDEX NAME)



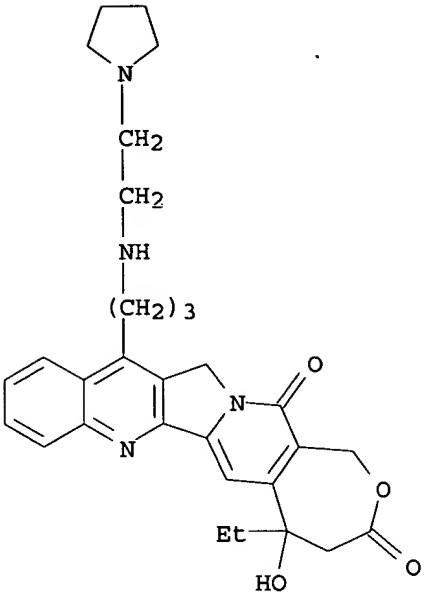
RN 360071-38-1 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[[[4-(hydroxymethyl)-1-piperazinyl]amino]methyl]- (9CI) (CA INDEX NAME)



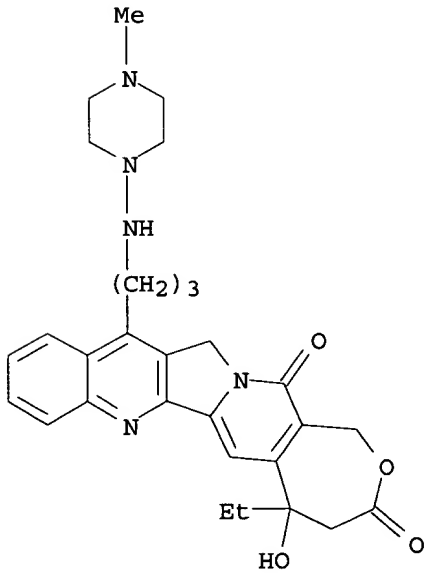
RN 360071-39-2 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[3-[[2-(4-morpholinyl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)



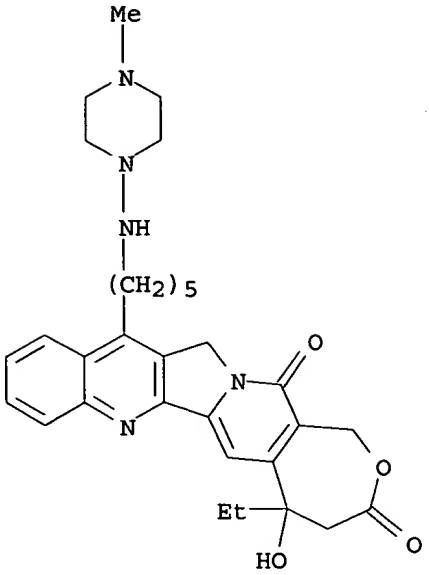
RN 360071-40-5 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[3-[[2-(1-pyrrolidinyl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)



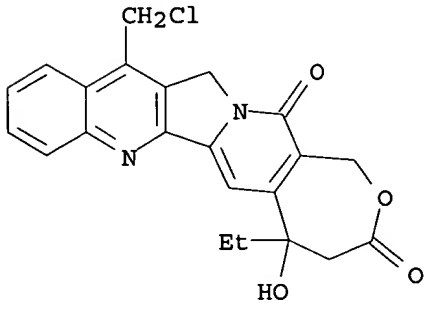
RN 360071-41-6 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[3-[(4-methyl-1-piperazinyl)amino]propyl]- (9CI) (CA INDEX NAME)



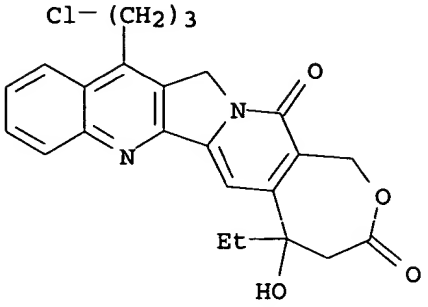
RN 360071-42-7 USPATFULL
CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[5-[(4-methyl-1-piperazinyl)amino]pentyl]- (9CI) (CA INDEX NAME)



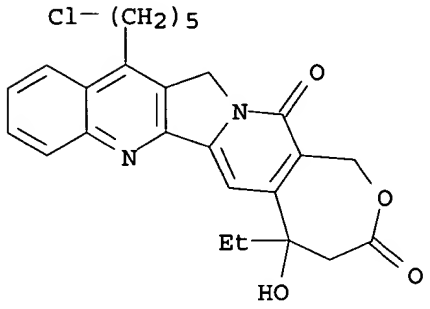
IT **360071-30-3P 360071-31-4P 360071-32-5P**
(prepn. of water-sol. camptothecin/homocamptothecin derivs.)
RN 360071-30-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(chloromethyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 360071-31-4 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3-chloropropyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 360071-32-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(5-chloropentyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



L7 ANSWER 3 OF 5 USPATFULL
AB A method of synthesizing a compound having the formula ##STR1##

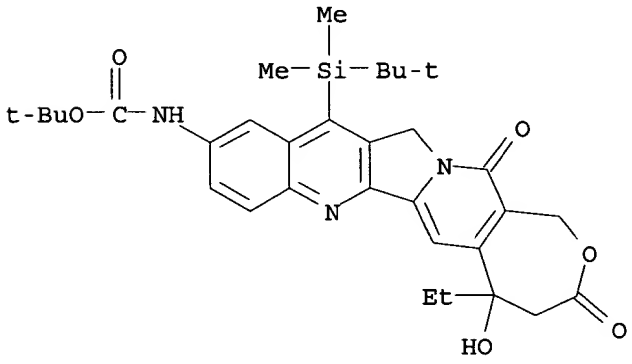
via a cascade radical 4+1 annulation includes the step wherein the precursor ##STR2##

is reacted with an arylisonitrile having the formula ##STR3##

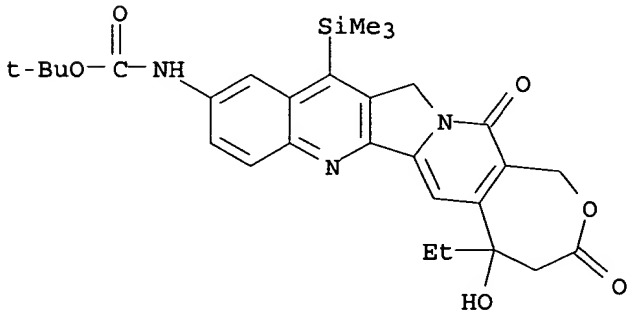
wherein X is a radical precursor such as Cl, Br or I. R.sup.6 is preferably --Si(R.sup.8R.sup.9R.sup.10) or --(R.sup.7)Si(R.sup.8R.sup.9R.sup.10), wherein R.sup.7 is an alkylene group, an alkenylene group, or an alkynylene group; and R.sup.8, R.sup.9 and R.sup.10 are independently a C.sub.1-10 alkyl group, a C.sub.2-10 alkenyl group, a C.sub.2-10 alkynyl group, an aryl group or a --(CH.sub.2).sub.NR.sup.11 group, wherein N is an integer within the range of 1 through 10 and R.sup.11 is a hydroxy group, alkoxy group, an amino group, an alkylamino group, a dialkylamino group, a halogen atom, a cyano group, --SR.sup.c or a nitro group. R.sup.1-R.sup.4 can be broadly substituted. R.sup.5 is preferably a C.sub.1-10 alkyl group, an alkenyl group, an alkynyl group, or a benzyl group. R.sup.13 is preferably H, F or --CH.sub.3. R.sup.16 is R.sup.16 is --C(O)R.sup.f or H. The E-ring (the lactone ring) may be opened.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:91628 USPATFULL
TI Camptothecin analogs and methods of preparation thereof

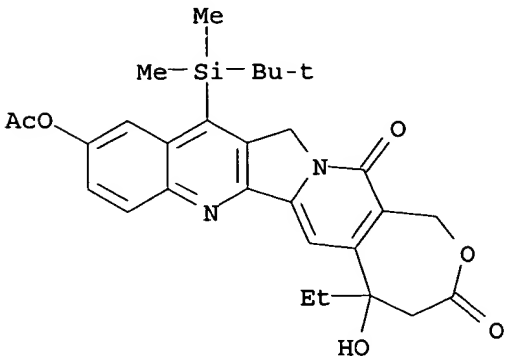
IN Curran, Dennis P., Pittsburgh, PA, United States
David, Bom, Pittsburgh, PA, United States
Burke, Thomas G., Lexington, KY, United States
PI US 2001003779 A1 20010614
AI US 2000-728031 A1 20001130 (9)
RLI Continuation of Ser. No. US 1999-290019, filed on 9 Apr 1999, PENDING
DT Utility
FS APPLICATION
LREP HENRY E. BARTONY, JR., BARTONY & HARE, SUITE 1801, LAW & FINANCE BUILDING, 429 FOURTH AVENUE, PITTSBURGH, PA, 15219
CLMN Number of Claims: 57
ECL Exemplary Claim: 1
DRWN 18 Drawing Page(s)
LN.CNT 2375
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **300582-81-4P 300582-89-2P 300582-92-7P 300582-93-8P**
(prepn. of camptothecin analogs for pharmaceutical use in the treatment of cancer)
RN 300582-81-4 USPATFULL
CN Carbamic acid, [12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



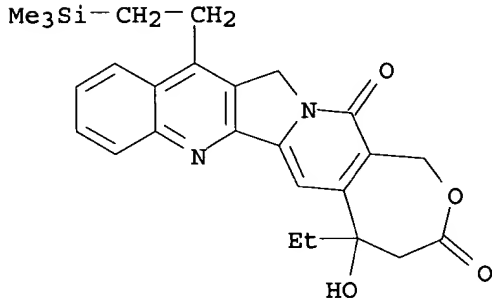
RN 300582-89-2 USPATFULL
CN Carbamic acid, [5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-12-(trimethylsilyl)-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 300582-92-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

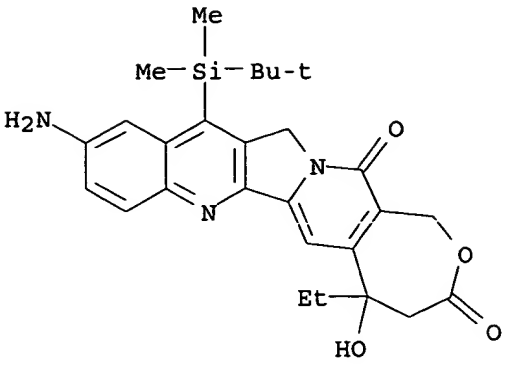


RN 300582-93-8 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)

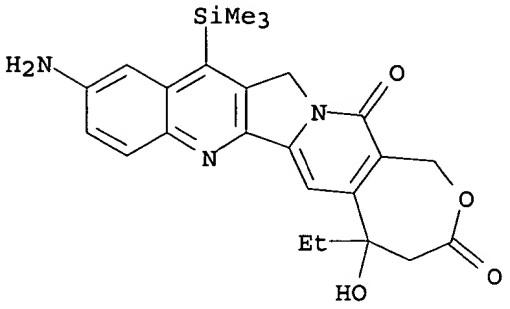


IT **247043-96-5P**, Camptothecin DB 90 **247043-97-6P**, DB 38
247043-98-7P, DB 91 **247043-99-8P**, DB 81
300582-87-0P 300582-91-6P 300582-94-9P
300582-96-1P 300582-98-3P 300582-99-4P
(prepn. of camptothecin analogs for pharmaceutical use in the treatment of cancer)

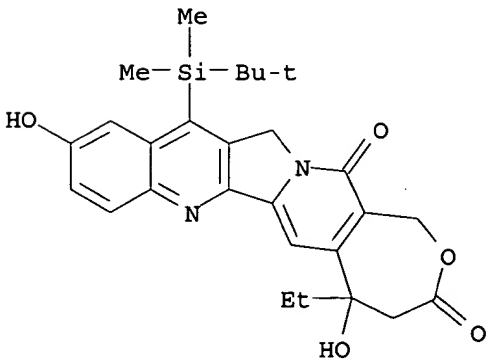
RN 247043-96-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



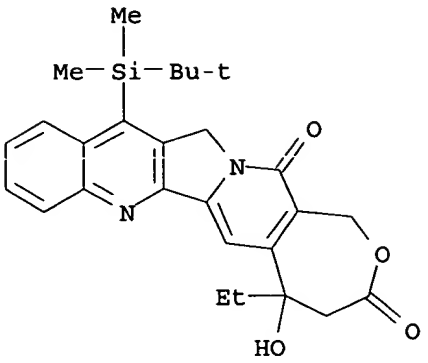
RN 247043-97-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



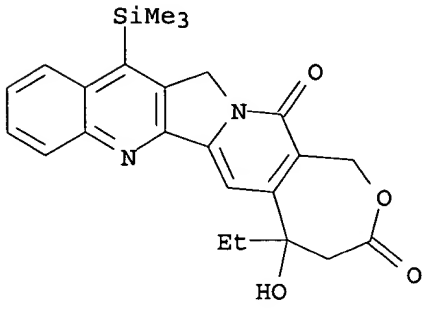
RN 247043-98-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



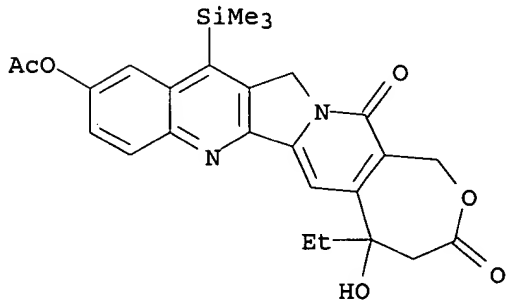
RN 247043-99-8 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



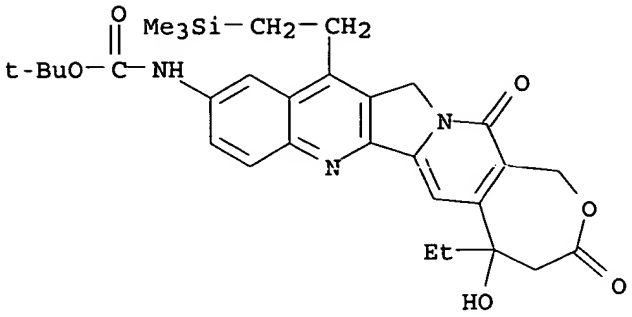
RN 300582-87-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



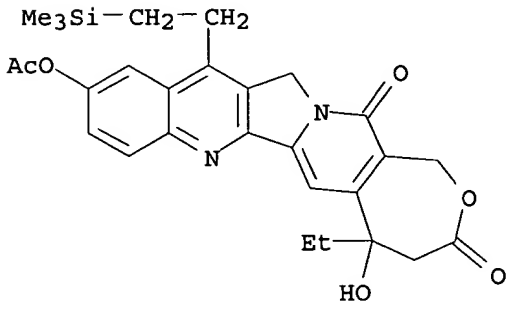
RN 300582-91-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



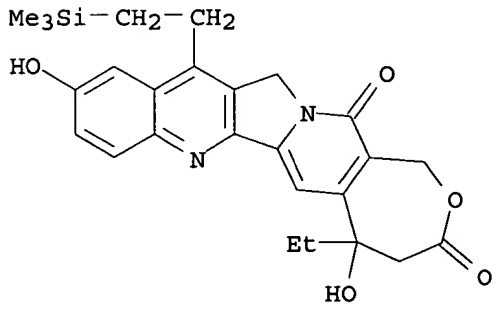
RN 300582-94-9 USPATFULL
CN Carbamic acid, [5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-12-[2-(trimethylsilyl)ethyl]-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



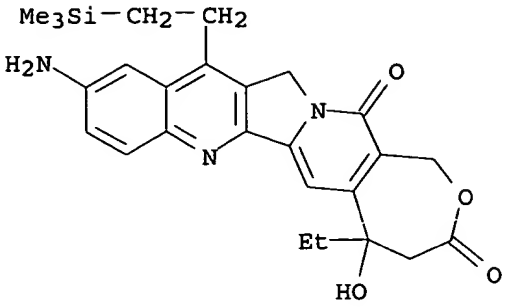
RN 300582-96-1 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



RN 300582-98-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



RN 300582-99-4 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)

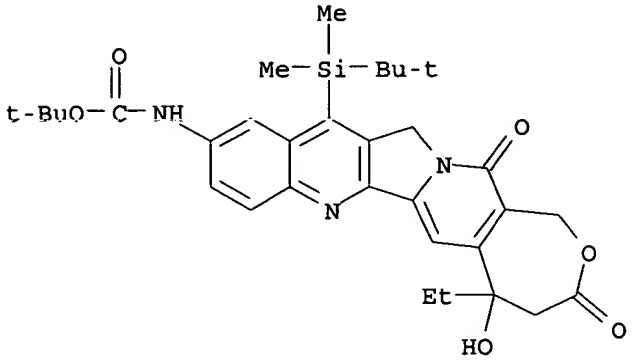


L7 ANSWER 4 OF 5 USPATFULL
AB A compound has the formula ##STR1##

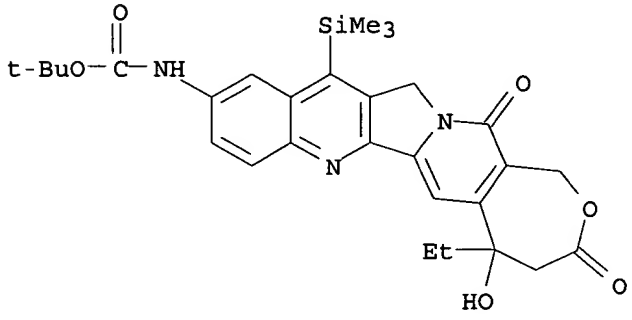
in racemic form, enantiomerically enriched form or enantiomerically pure form. R.sup.6 is preferably --Si(R.sup.8 R.sup.9 R.sup.10) or --(R.sup.7)Si(R.sup.8 R.sup.9 R.sup.10), wherein R.sup.7 is an alkylene group, an alkenylene group, or an alkynylene group; and R.sup.8, R.sup.9 and R.sup.10 are independently a C.sub.1-10 alkyl group, a C.sub.2-10 alkenyl group, a C.sub.2-10 alkynyl group, an aryl group or a --(CH.sub.2).sub.N R.sup.11 group, wherein N is an integer within the range of 1 through 10 and R.sup.11 is a hydroxy group, alkoxy group, an amino group, an alkylamino group, a dialkylamino group, a halogen atom, a cyano group, --SR.sup.c or a nitro group. R.sup.1 -R can be broadly substituted. R.sup.5 is preferably a C.sub.1-10 alkyl group, an alkenyl group, an alkynyl group, or a benzyl group. R.sup.13 is preferably H, F or --CH.sub.3. R.sup.16 is R.sup.16 is --C(O)R.sup.f or H. The E-ring (the lactone ring) may be opened. A method of synthesis of compound (1) and intermediates in the synthesis thereof are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:44389 USPATFULL
TI Camptothecin analogs and methods of preparation thereof
IN Curran, Dennis P., Pittsburgh, PA, United States
David, Bom, Pittsburgh, PA, United States
Burke, Thomas G., Lexington, KY, United States
PA University of Pittsburgh, Pittsburgh, PA, United States (U.S. corporation)
PI US 6207832 B1 20010327
AI US 1999-290019 19990409 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Aulakh, Charanjit S.
LREP Bartony & Hare
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 18 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 2187
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **300582-81-4P 300582-89-2P 300582-92-7P 300582-93-8P**
(prepn. of camptothecin analogs for pharmaceutical use in the treatment of cancer)
RN 300582-81-4 USPATFULL
CN Carbamic acid, [12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-

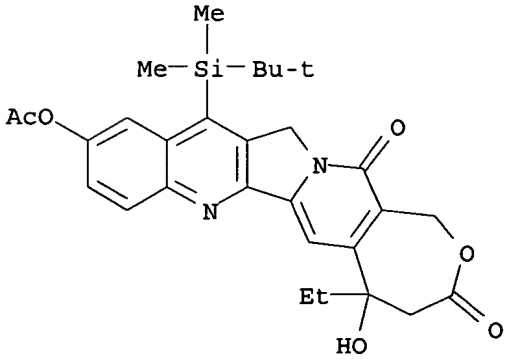
b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 300582-89-2 USPATFULL
CN Carbamic acid, [5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-12-(trimethylsilyl)-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

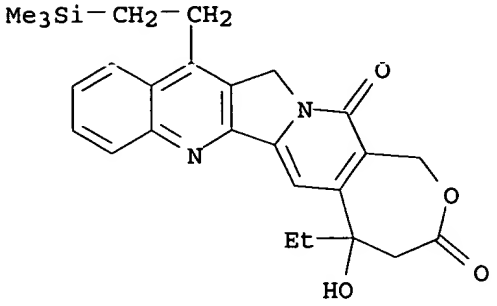


RN 300582-92-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 300582-93-8 USPATFULL

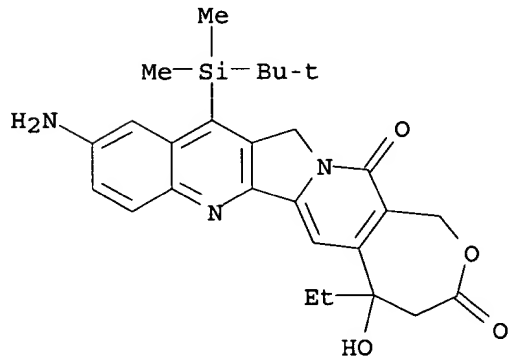
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



IT **247043-96-5P**, Camptothecin DB 90 **247043-97-6P**, DB 38
247043-98-7P, DB 91 **247043-99-8P**, DB 81
300582-87-0P 300582-91-6P 300582-94-9P
300582-96-1P 300582-98-3P 300582-99-4P
(prepn. of camptothecin analogs for pharmaceutical use in the treatment of cancer)

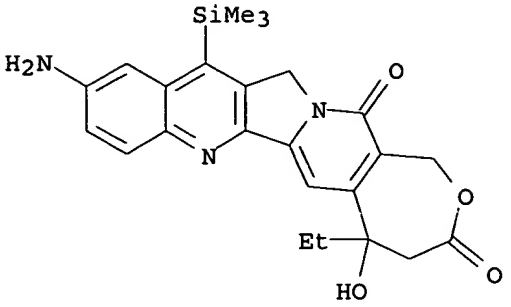
RN 247043-96-5 USPATFULL

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

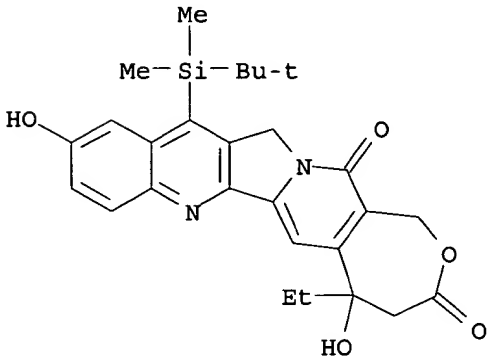


RN 247043-97-6 USPATFULL

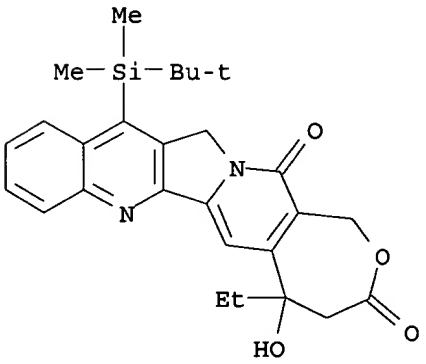
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



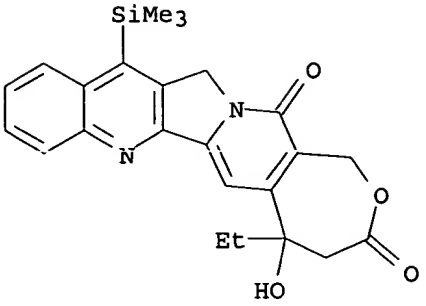
RN 247043-98-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



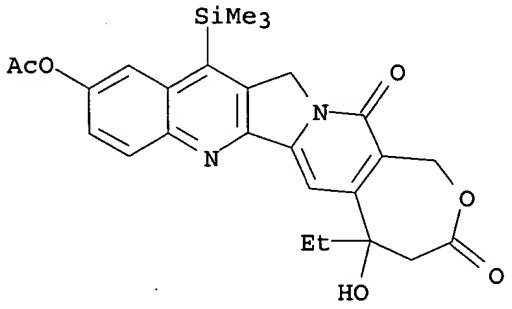
RN 247043-99-8 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



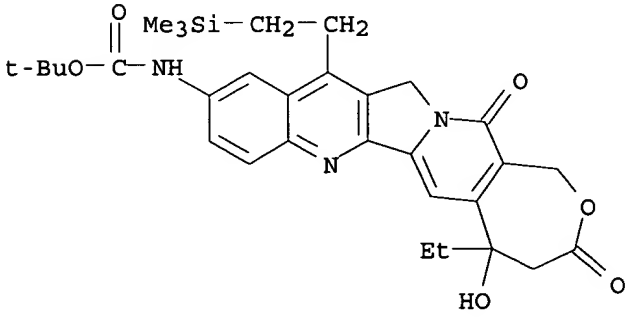
RN 300582-87-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



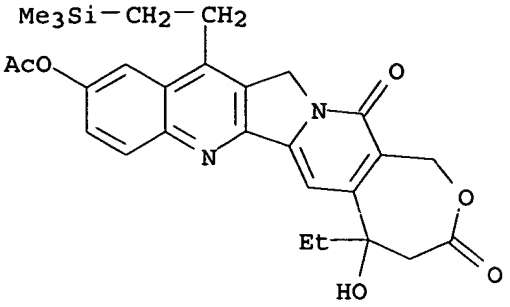
RN 300582-91-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



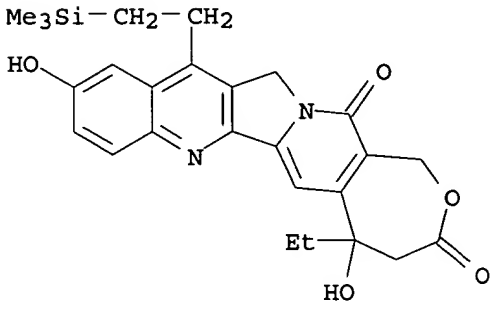
RN 300582-94-9 USPATFULL
CN Carbamic acid, [5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-12-[2-(trimethylsilyl)ethyl]-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



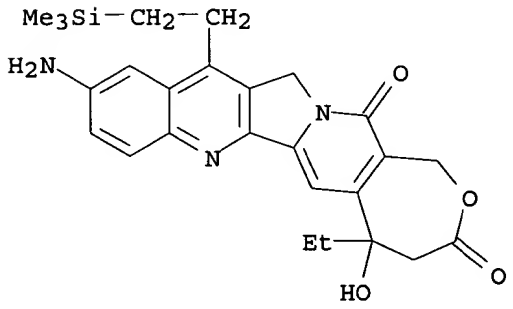
RN 300582-96-1 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



RN 300582-98-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



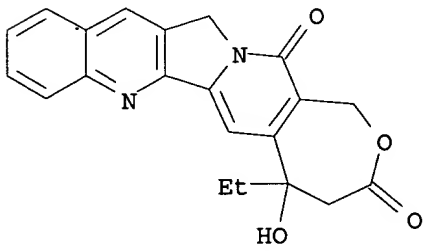
RN 300582-99-4 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



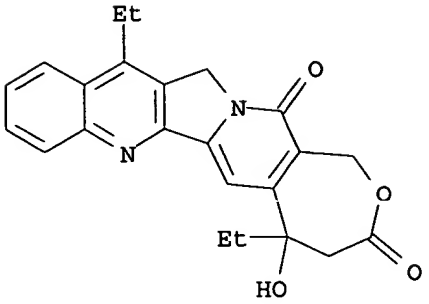
L7 ANSWER 5 OF 5 USPATFULL
AB A camptothecin analog characterized in that the hydroxy lactone of the camptothecin is a .beta.-hydroxy lactone or the corresponding .beta.-hydroxyacid, resulting from the opening of said lactone, or a derivative of said .beta.-hydroxyacid, or a Pharmaceutically acceptable salt thereof, is disclosed. In particular, compounds of formulae (I) and (II) are disclosed. Methods for preparing the compounds of formulae (I)

and (II), pharmaceutical compositions containing said containing said compounds, and their use, particularly as topoisomerase inhibitors and antitumoral drugs, are also disclosed.

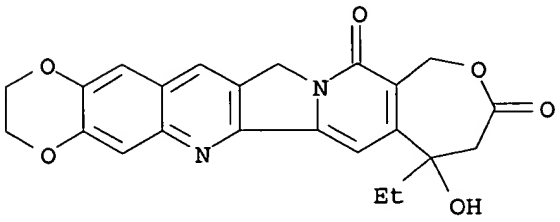
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1999:141949 USPATFULL
TI Camptothecin analogues, preparation methods therefor, use thereof as drugs, and pharmaceutical compositions containing said analogues
IN Bigg, Dennis, Gif-sur-Yvette, France
Lavergne, Olivier, Massy, France
Pla Rodas, Francesc, Santa Coloma de Farners, Spain
Pommier, Jacques, Colombes, France
Ulibarri, Gerard, Bures-sur-Yvette, France
PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S.), France (non-U.S. corporation)
PI US 5981542 19991109
WO 9700876 19970109
AI US 1997-973561 19971202 (8)
WO 1996-FR980 19960621
19971202 PCT 371 date
19971202 PCT 102(e) date
PRAI GB 1995-12670 19950621
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Kifle, Bruck
LREP Bierman, Muserlian and Lucas
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **186668-40-6P 186668-44-0P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-40-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



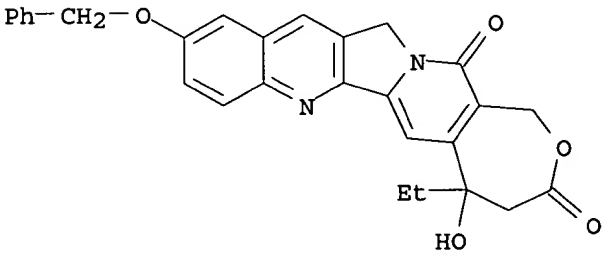
RN 186668-44-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



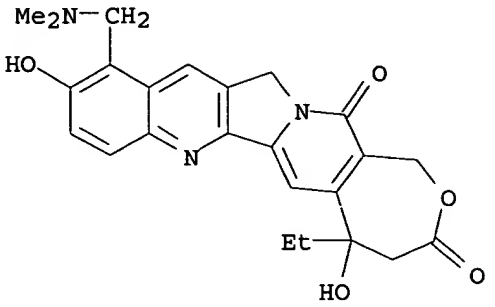
IT **186668-59-7P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-59-7 USPATFULL
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)



IT **186668-63-3P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-63-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)



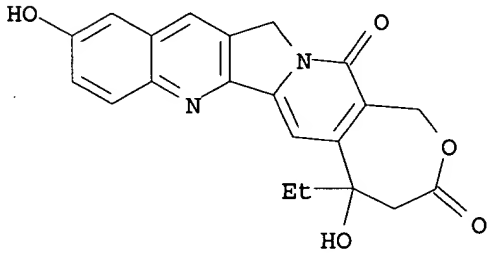
IT **186668-66-6P**
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-66-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



IT **186668-65-5P 186668-67-7P 186668-68-8P**
186668-69-9P 186668-70-2P 186668-71-3P
186668-72-4P 186668-73-5P 186668-74-6P
186668-75-7P 186668-77-9P 186668-79-1P
186668-81-5P 186668-83-7P 186668-90-6P
186668-94-0P 186669-03-4P 186669-04-5P
186669-06-7P 186669-07-8P 186669-08-9P
186669-09-0P 186669-10-3P 186669-12-5P
186669-13-6P 186669-14-7P 186669-16-9P
186669-18-1P 186669-19-2P 186669-20-5P
(prepn. of camptothecin analogs as antitumor agents)

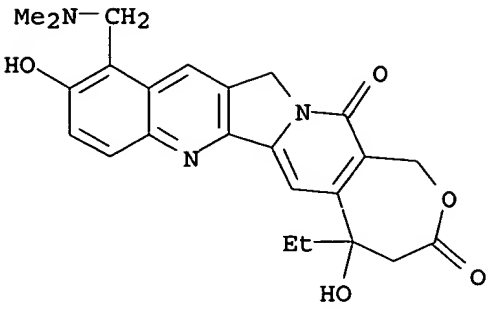
RN 186668-65-5 USPATFULL

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



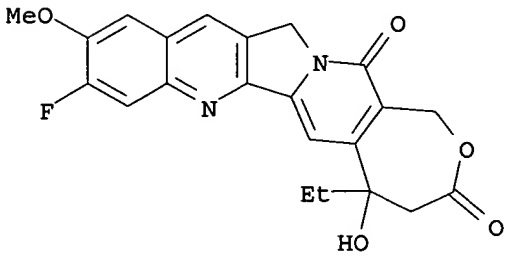
RN 186668-67-7 USPATFULL

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

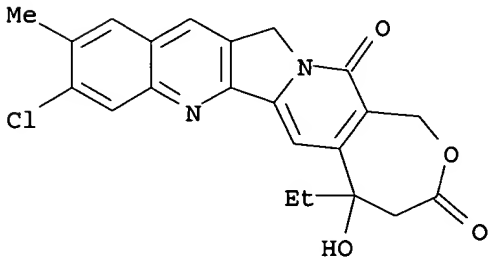


● HCl

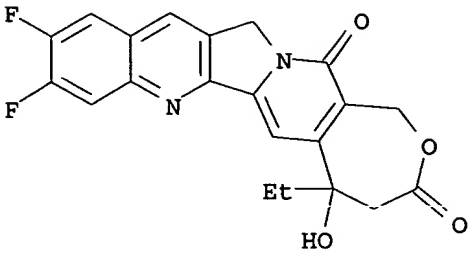
RN 186668-68-8 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



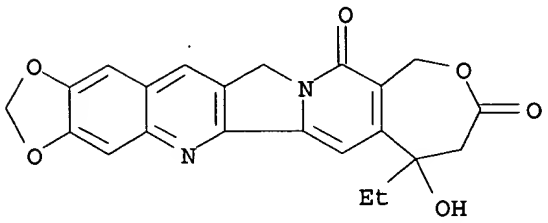
RN 186668-69-9 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



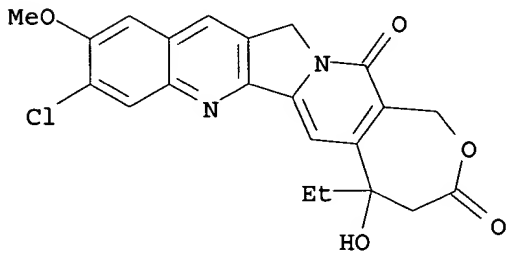
RN 186668-70-2 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



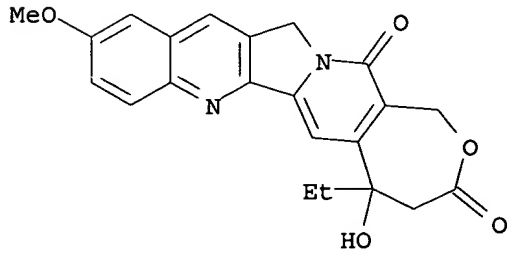
RN 186668-71-3 USPATFULL
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)



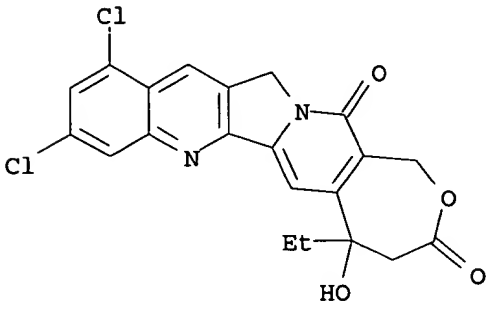
RN 186668-72-4 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



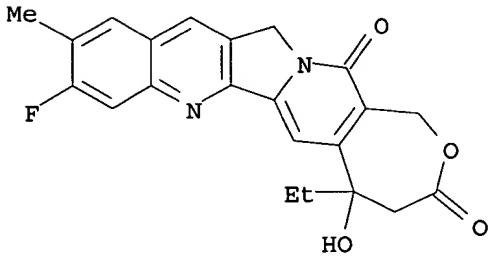
RN 186668-73-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



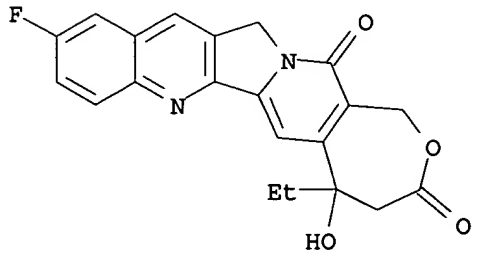
RN 186668-74-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9,11-dichloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



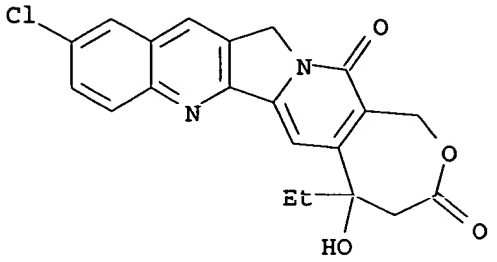
RN 186668-75-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



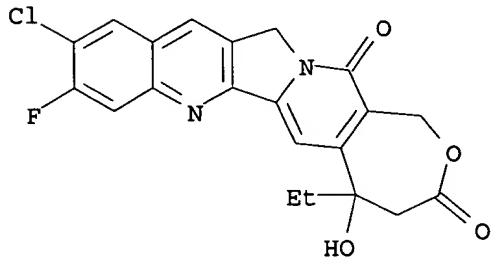
RN 186668-77-9 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



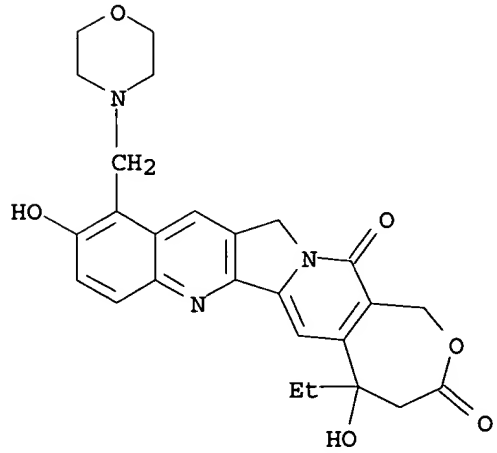
RN 186668-79-1 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



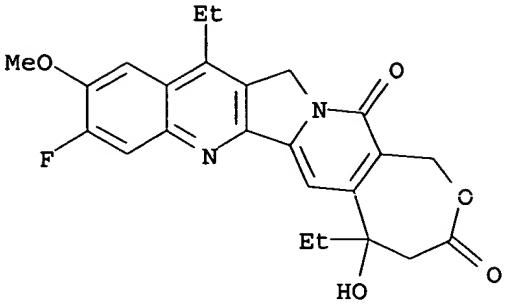
RN 186668-81-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



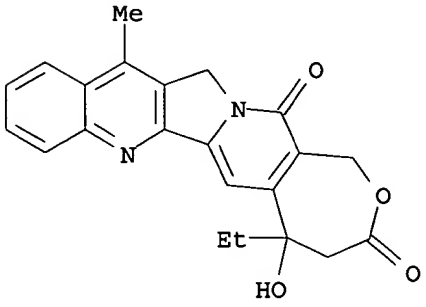
RN 186668-83-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-11-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



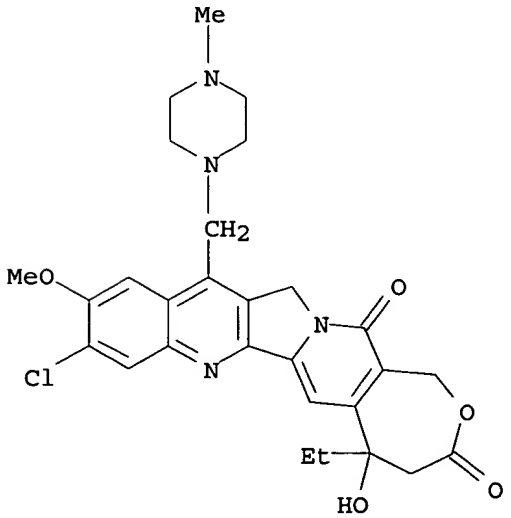
RN 186668-90-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



RN 186668-94-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-methyl- (9CI) (CA INDEX NAME)

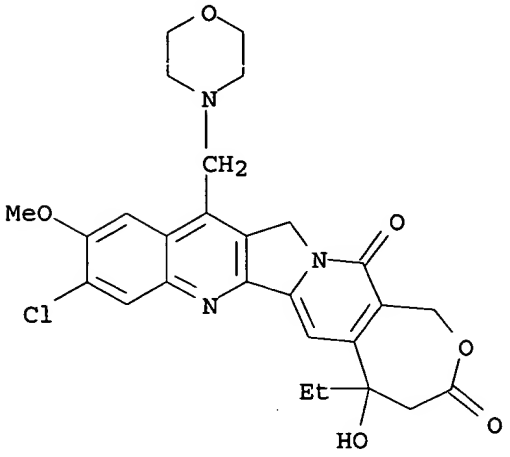


RN 186669-03-4 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

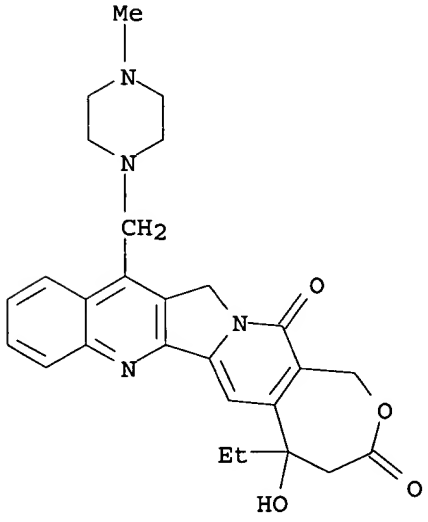


RN 186669-04-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

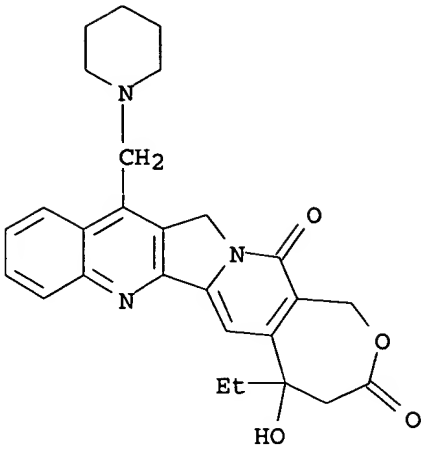
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



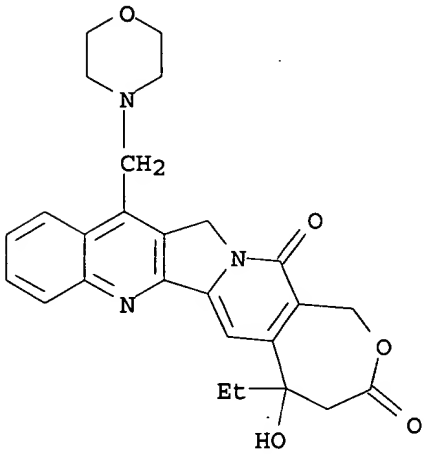
RN 186669-06-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



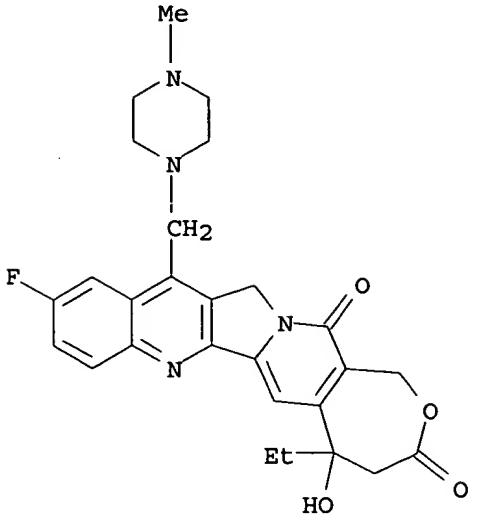
RN 186669-07-8 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



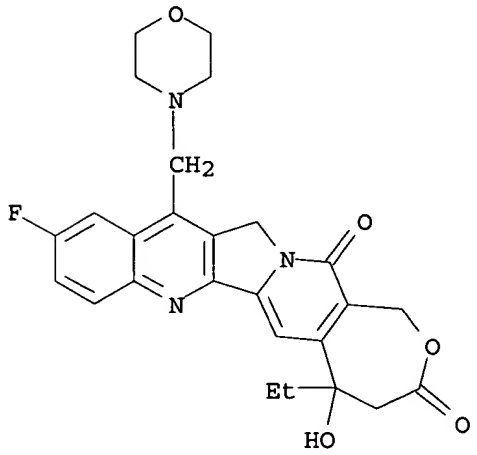
RN 186669-08-9 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



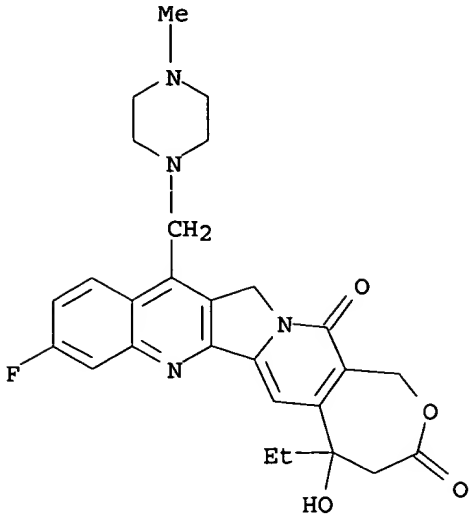
RN 186669-09-0 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



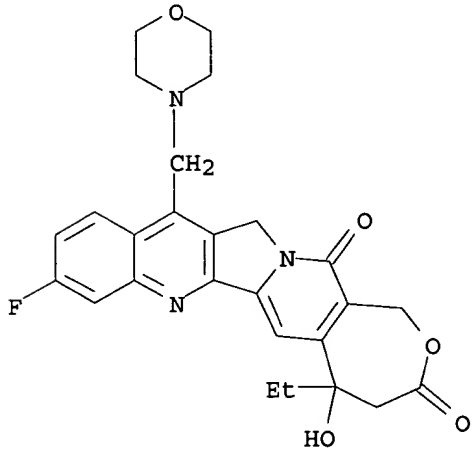
RN 186669-10-3 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



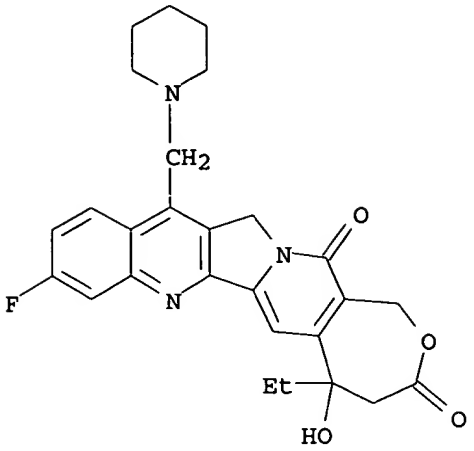
RN 186669-12-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



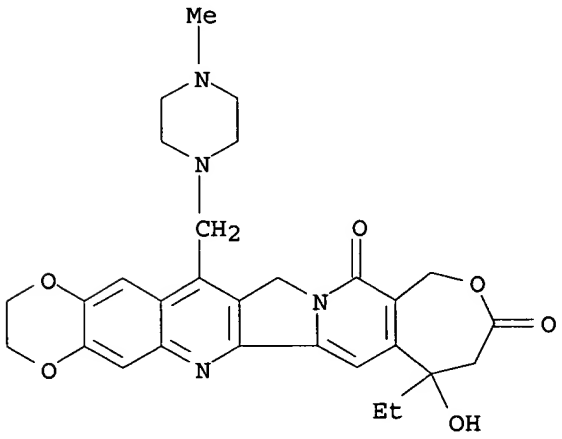
RN 186669-13-6 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)-
(9CI) (CA INDEX NAME)



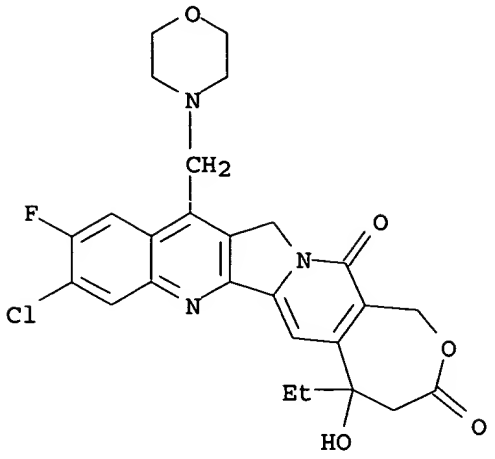
RN 186669-14-7 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)-
(9CI) (CA INDEX NAME)



RN 186669-16-9 USPATFULL
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy-16-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

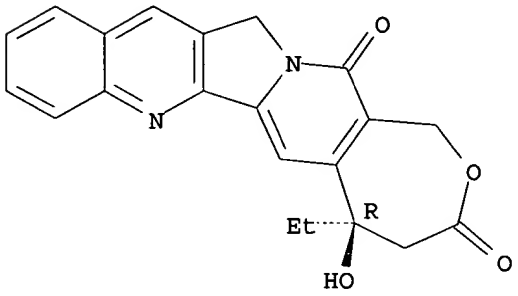


RN 186669-18-1 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



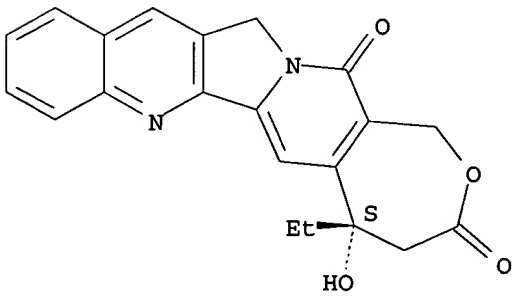
RN 186669-19-2 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186669-20-5 USPATFULL
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Print selected from Online session13/12/2001

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L8 23 L6

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L8 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2001 ACS
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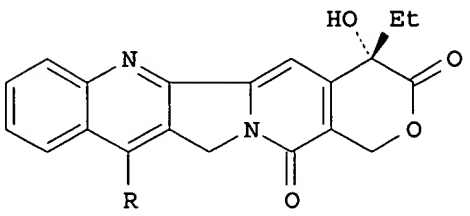

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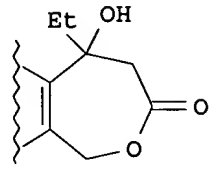
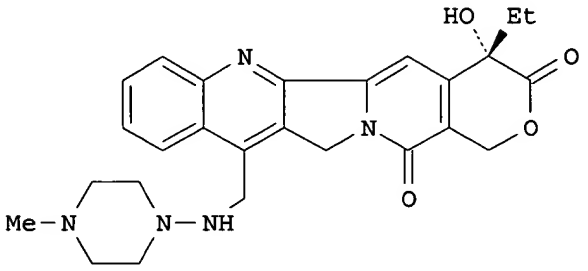


II



III

AB Camptothecin and homocamptothecin analogs and derivs. of formulas I and II [R = (substituted) C1-20 alkyl-NH2] are provided incorporating alkylamine and polyalkylamine moieties. The compds. have high antitumor activity and water-soly. and minimal toxicity. Thus, CT-17 (III) was prepd. from camptothecin.

AN 2001:687480 CAPLUS
DN 135:242387
TI Preparation of water-soluble derivatives of camptothecin/homocamptothecin
IN Burke, Thomas G.; Demir, Ayhan S.; Tanyeli, Cihangir; Chavan, Ashok J.; Wang, Tie-Lin; Pommier, Yves
PA University of Kentucky Research Foundation, USA
SO U.S., 36 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

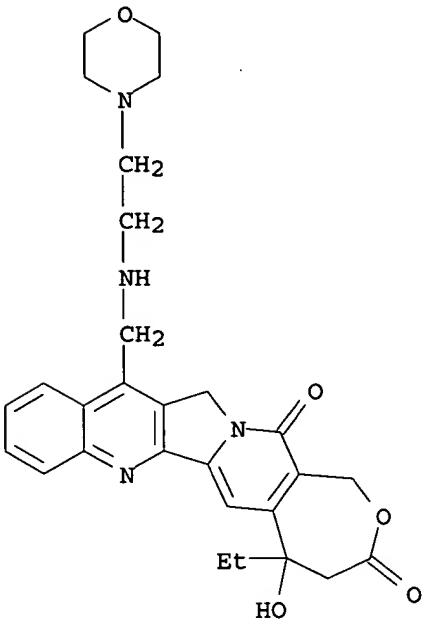
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6291676	B1	20010918	US 2000-517210	20000302

PRAI US 1999-122621 P 19990303
OS MARPAT 135:242387
IT **360071-33-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of water-sol. camptothecin/homocamptothecin derivs.)

RN 360071-33-6 CAPLUS

CN 1H,3H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(13H)-dione, 5-ethyl-4,5-dihydro-5-hydroxy-12-[[[2-(4-morpholinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)



RE.CNT 10

RE

(2) Burke; US 5552156 1996 CAPLUS

(3) Danishefsky; US 5446047 1995 CAPLUS

(4) Danishefsky; US 5525731 1996 CAPLUS

(6) Lackey; US 5342947 1994 CAPLUS

(8) Sawada; Chem Pharm Bull 1991, V39(10), P2574 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB The homocamptothecin (hCPT) deriv. BN80915 contg. a seven-membered lactone ring represents one of the most potent topoisomerase I inhibitors described. This anticancer agent, currently undergoing phase I clin. trials, has been shown to produce a greater no. of DNA strand breaks than conventional camptothecins with a six-membered lactone ring. To shed light on the mechanism of action of hCPT at the cellular level, we compared the effects of BN80915 and the classic camptothecin SN-38, the active metabolite of irinotecan, on HL-60 human promyelocytic cancer cells. A variety of biochem. events, at both the mitochondrial and the nuclear levels, were characterized to det. how and to what extent the hCPT deriv. can induce apoptotic cell death. The use of cytometry, Western blot anal., confocal microscopy, and different colorimetric assays enabled us to demonstrate that BN80915 is a potent inducer of apoptosis in HL-60 cells. This induction of apoptosis is assocd. with cell cycle changes, a marked decrease of intracellular pH, activation of caspase-3 and -8, DNA fragmentation, and externalization of phosphatidylserine lipids but no

significant changes of the mitochondrial membrane potential or the expression of Bcl-2. The interconnections between these different events are discussed. Collectively, the results indicate that the superior activity expressed at the topoisomerase I level leads to a more pronounced induction of apoptosis by BN80915 compared with SN-38. The study identifies and delineates signaling factors involved in BN80915-induced apoptosis in HL-60 cells.

AN 2001:612480 CAPLUS

TI Apoptosis induced by the homocamptothecin anticancer drug BN80915 in HL-60 cells

AU Lansiaux, Amelie; Facompre, Michael; Wattez, Nicole; Hildebrand, Marie-Paule; Bal, Christine; Demarquay, Daniele; Lavergne, Olivier; Bigg, Dennis C. H.; Bailly, Christian

CS Institut National de la Sante et de la Recherche Medicale U-524 and Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, Institut de Recherche sur le Cancer de Lille, Lille, Fr.

SO Mol. Pharmacol. (2001), 60(3), 450-461
CODEN: MOPMA3; ISSN: 0026-895X

date not good

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

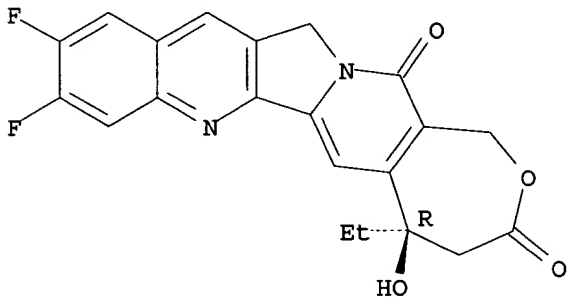
LA English

IT **220997-97-7**, BN80915
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis induced by homocamptothecin anticancer drug BN80915 in HL-60 cells)

RN 220997-97-7 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 45

RE

(1) Antonsson, B; Exp Cell Res 2000, V256, P50 CAPLUS

(3) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS

(4) Bom, D; J Med Chem 1999, V42, P3018 CAPLUS

(5) Bossy-Wetzel, E; Methods Enzymol 2000, V322, P15 CAPLUS

(7) Daugas, E; FEBS Lett 2000, V476, P118 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2001 ACS

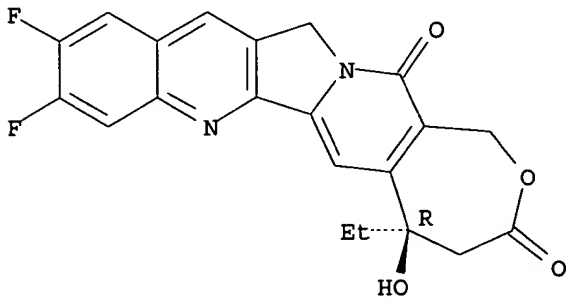
AB BN 80915 is the lead compd. from a novel class of E-ring modified camptothecin analogs, the homocamptothecins, which show potent antitumor activities in animal models. Here, we report that BN 80915 induces up to

2-fold more cleavable complexes between plasmid DNA and purified human topoisomerase I than SN-38 and camptothecin. BN 80915 also induces DNA-topoisomerase I complexes in living HT-29 colon carcinoma cells, as shown by the in vivo link assay. BN 80915 is an extremely potent inducer of DNA-protein complexes in these cells starting at a concn. of 5 nM in the media. BN 80915 is clearly more potent than SN-38, because at least 20 times more SN-38 is needed to induce comparable levels of cleavable complexes. Kinetic expts. show that BN 80915 induces cleavable complexes within minutes that remain stable for at least 6 h in the presence of drug. Whereas the majority of the complexes are reversed within 15 min after drug removal, a substantial fraction (30%) persists for at least 4 h, in contrast with SN-38-treated cells, where all complexes have disappeared by this time. BN 80915 shows strong antiproliferative effects toward HT-29 cells with an IC50 of 0.3 nM compared with 20 nM for SN-38 and 40 nM for topotecan. BN 80915 is also potent against other colon carcinoma cells as well as toward cells growing in three dimensions as multicellular spheroids. HL-60 cells expressing functional P-glycoprotein or multidrug resistance protein show no cross-resistance toward BN 80915. Taken together, our results show that BN 80915 is unusually potent toward human colon carcinoma cells because of the formation of high levels of stable, covalent DNA-topoisomerase complexes.

AN 2001:295908 CAPLUS
DN 135:86702
TI Unusual potency of BN 80915, a novel fluorinated E-ring modified camptothecin, toward human colon carcinoma cells
AU Larsen, Annette K.; Gilbert, Cristele; Chyzak, Ginette; Plisov, Sergey Y.; Naguibneva, Irina; Lavergne, Olivier; Lesueur-Ginot, Laurence; Bigg, Dennis C. H.
CS Centre National de la Recherche Scientifique UMR 8532, Institut Gustave-Roussy, Villejuif, F-94805, Fr.
SO Cancer Res. (2001), 61(7), 2961-2967
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
IT **220997-97-7**, BN 80915
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potency of BN80915 toward human colon carcinoma cells)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

date not good

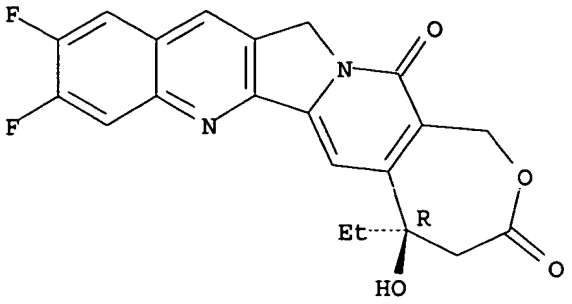
Absolute stereochemistry. Rotation (+).



RE.CNT 49
RE
(1) Aktipis, S; Biochemistry 1974, V13, P112 CAPLUS
(2) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(3) Beidler, D; Mol Pharmacol 1995, V47, P907 CAPLUS
(5) Bom, D; J Med Chem 1999, V42, P3018 CAPLUS
(6) Burke, T; Ann NY Acad Sci 1996, V803, P29 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

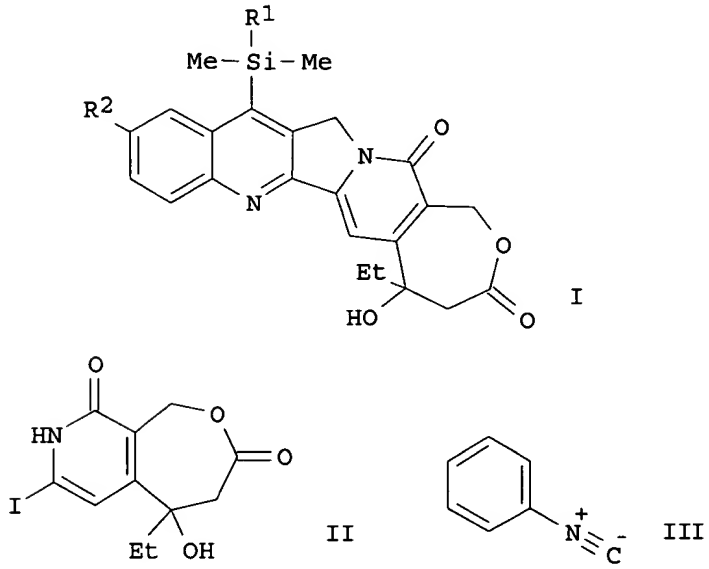
L8 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB BN 80915, a lead compd. of the homocamptothecin (hCPT) family, has entered clin. trials. BN 80915 is a difluoro-hCPT where the six-membered .alpha.-hydroxylactone ring of camptothecin (CPT) is replaced by a seven-membered .beta.-hydroxylactone ring. Preclin. data reported here show that in spite of the modification to the crucial E-ring of CPTs, BN 80915 retains topoisomerase I poisoning activity as shown in living HT29 cells as well as in cell-free assays, where BN 80915 always performs better than SN-38 or TPT. In antiproliferative assays BN 80915 is also very potent as evidenced by IC50s values consistently lower than those of SN38 in sensitive cell lines as well as in their related multidrug-resistant lines overexpressing P-glycoprotein or multidrug resistance-assocd. protein. Furthermore, in human plasma, in contrast to CPT analogs, the hydrolysis of BN 80915 is slow, leading to improved plasma stability, and irreversible, thus avoiding toxicity related to the accumulation of active principle during excretion in the urinary tract. These findings may account for the good in vivo efficacy obsd. in PC3 xenograft expts. where BN 80915 administered orally at very low doses doubled the tumor growth delay in comparison to CPT-11 administered i.p. Altogether, these results strongly support further development of BN 80915.
AN 2001:125578 CAPLUS
DN 134:348033
TI The homocamptothecin BN 80915 is a highly potent orally active topoisomerase I poison
AU Demarquay, Daniele; Huchet, Marion; Coulomb, Helene; Lesueur-Ginot, Laurence; Lavergne, Olivier; Kasprzyk, Philip G.; Bailly, Christian; Camara, Jose; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Anti-Cancer Drugs (2001), 12(1), 9-19
CODEN: ANTDEV; ISSN: 0959-4973
data not good
PB Lippincott Williams & Wilkins
DT Journal
LA English
IT **220997-97-7**, BN 80915
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecin BN 80915 is a highly potent orally active topoisomerase I poison in treatment of refractory tumors)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 42
RE
(1) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(2) Burris, H; Semin Hematol 1999, V36, P26 CAPLUS
(3) Cordobes, M; J Nucl Med 1996, V37, P286 CAPLUS
(4) Cunningham, D; Semin Oncol 1999, V26, P1 CAPLUS
(5) DeMario, M; J Clin Oncol 1998, V16, P2557 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2001 ACS
GI

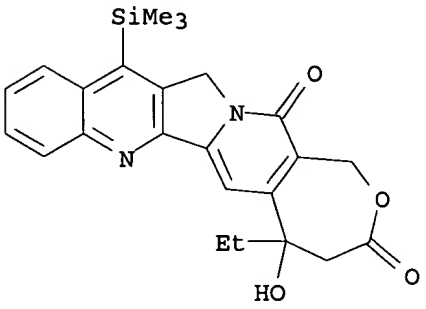


I

II III

AB The authors have developed a practical method for the prepn. of diverse homosilatecan analogs, I (R1 = straight hydrocarbon chain, branched hydrocarbon chain, or aryl group and R2 = H, F, MeO, Me, CF3 or AcO). N-Alkylation of iodopyridone II with different propargyl bromides gave compds. that were subjected to a cascade radical annulation with different aryl isonitriles, e.g. III, to give racemic homosilatecans, e.g. I, with two different elements of diversity. More than 100 racemic homosilatecans were prepd. by this radical annulation reaction by either the traditional way or a Hewlett-Packard soln. phase synthesizer.
AN 2001:70498 CAPLUS

DN 134:266468
TI The combinatorial synthesis of racemic homosilatecan libraries via a cascade radical annulation
AU Du, Wu; Gabarda, Ana E.; Bom, David; Curran, Dennis P.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Ann. N. Y. Acad. Sci. (2000), 922(Camptothecins), 317-319
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
IT **300582-87-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(combinatorial synthesis of racemic homosilatecan libraries via a cascade radical annulation)
RN 300582-87-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)

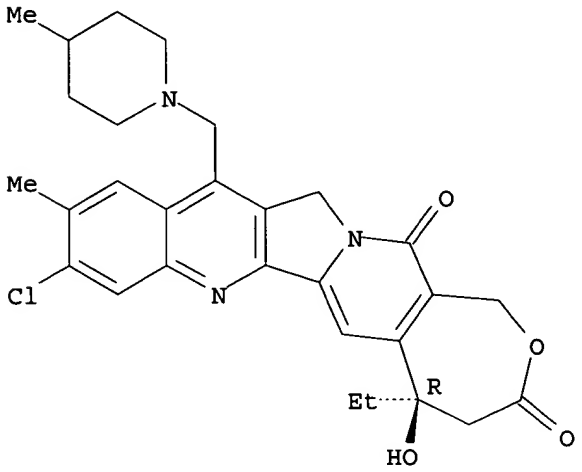


RE.CNT 9
RE
(1) Bom, D; J Med Chem 1999, V42, P3018 CAPLUS
(3) Burke, T; J Am Chem Soc 1992, V114, P8318 CAPLUS
(4) Hertzberg, R; Biochemistry 1989, V28, P4629 CAPLUS
(5) Hsiang, Y; Cancer Res 1988, V48, P1722 CAPLUS
(7) Josien, H; Chem Eur J 1998, V4, P67 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB A review with 2 refs. focusing on the results of studies on BN 80927 which belongs to a novel family of camptothecin analogs. Findings have shown that the drug is a potent inhibitor of tumor cell proliferation; it shows cytotoxic activity towards resting HT29 cells; and it induces tumor regression in xenograft models.
AN 2001:70494 CAPLUS
DN 135:86401
TI The dual topoisomerase inhibitor, BN 80927, is highly potent against cell proliferation and tumor growth
AU Huchet, Marion; Demarquay, Daniele; Coulomb, Helene; Kasprzyk, Philip; Carlson, Mark; Lauer, Jeffrey; Lavergne, Olivier; Bigg, Dennis
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Ann. N. Y. Acad. Sci. (2000), 922(Camptothecins), 303-305
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences

DT Journal; General Review
LA English
IT **220997-99-9**, BN 80927
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual topoisomerase inhibitor BN 80927 is highly potent against cell proliferation and tumor growth)
RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RE.CNT 2
RE
(1) Lavergne, O; Bioorg Med Chem Lett 1999, V9, P2599 CAPLUS
(2) Lavergne, O; J Med Chem 1998, V41, P5410 CAPLUS

L8 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB Homocamptothecins (hCPTs) represent a new family of camptothecin analogs in which insertion of a methylene spacer between the alc. moiety and carbonyl group of the classical six-membered .alpha.-hydroxylactone ring results in a seven-membered .beta.-hydroxylactone ring which undergoes slow and irreversible hydrolytic ring-opening, providing higher plasma concns. of the active lactone form. Homocamptothecins have been shown to be highly potent antitumor drugs in vitro and in vivo, acting via a classical topoisomerase I poisoning mechanism. Structure activity studies led to the selection of a difluorinated hCPT, BN 80915, which is now in clin. trials. Interestingly, another promising hCPT, BN 80927, which shows inhibitory effects of topoisomerase II activity in addn. to its topoisomerase I poisoning activity, has been discovered. The results are discussed in relation to the antitumor activity of BN 80927.
AN 2001:70493 CAPLUS
DN 135:86664
TI The homocamptothecin, BN 80927, is a potent topoisomerase I poison and

topoisomerase II catalytic inhibitor

AU Demarquay, Daniele; Coulomb, Helene; Huchet, Marion; Lesueur-Ginot, Laurence; Camara, Jose; Lavergne, Olivier; Bigg, Dennis
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.

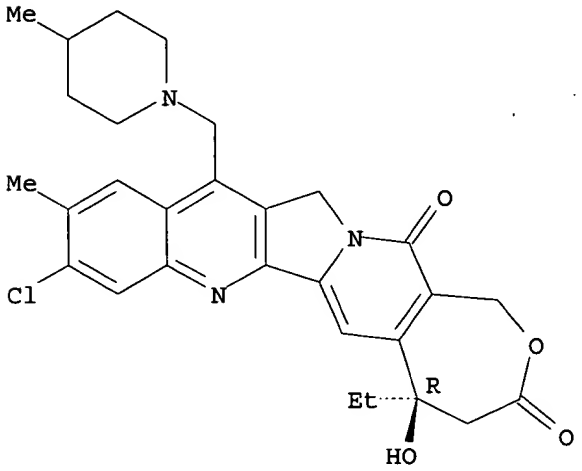
SO Ann. N. Y. Acad. Sci. (2000), 922(Camptothecins), 301-302
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English

date - not good

IT **220997-99-9**, BN 80927
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecin BN 80927 is a potent topoisomerase I poison and topoisomerase II catalytic inhibitor in relation to antitumor activity)

RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

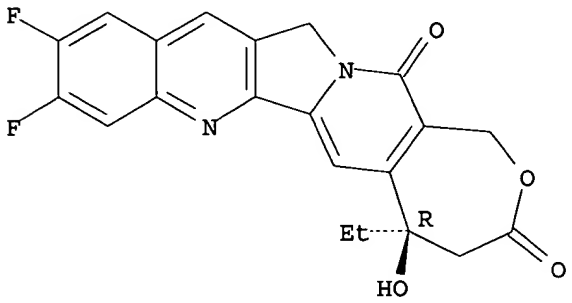
RE.CNT 5
RE
(1) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(2) Lavergne, O; Bioorg Med Chem Lett 1997, V7, P2235 CAPLUS
(3) Lavergne, O; Bioorg Med Chem Lett 1999, V9, P2599 CAPLUS
(4) Lavergne, O; J Med Chem 1998, V41, P5410 CAPLUS
(5) Lesueur-Ginot, L; Cancer Res 1999, V59, P2939 CAPLUS

L8 ANSWER 8 OF 23 CAPLUS
AB A review with 18 refs. Homocamptothecins (hCPT) are modified camptothecins (CPT) with a seven-membered .beta.-hydroxylactone instead of the naturally occurring six-membered .alpha.-hydroxylactone. This E-ring modification fully conserves the ability to stabilize topo I-DNA single-strand breaks and stimulates high levels of DNA cleavage. A key feature is the irreversibility of E-ring opening, which should give

reduced toxicity. Substituted hCPTs have been selected for their high antiproliferative activity on a panel of tumor cell lines, including those with cross resistance, and were active at very low doses in a variety of human tumor xenografts when administered orally. BN 80915, a difluoro-hCPT, has entered clin. trials.

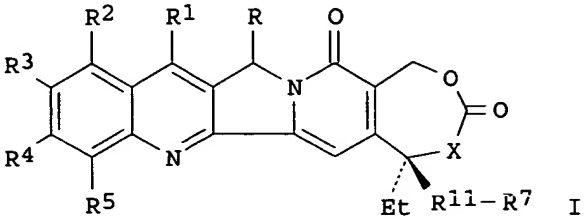
AN 2001:70474 CAPLUS
DN 135:101743
TI Homocamptothecins: E-ring modified CPT analogues
AU Lavergne, Olivier; Demarquay, Daniele; Kasprzyk, Philip G.; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Ann. N. Y. Acad. Sci. (2000), 922(Camptothecins), 100-111
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal; General Review
LA English
IT **220997-97-7**, BN 80915
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecins: E-ring modified CPT analogs)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 18
RE
(1) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(2) Comins, D; J Am Chem Soc 1992, V114, P10971 CAPLUS
(3) Fan, Y; J Med Chem 1998, V41, P2216 CAPLUS
(6) Hertzberg, R; Biochemistry 1989, V28, P4629 CAPLUS
(7) Holm, C; Cancer Res 1989, V49, P6365 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2001 ACS
GI



I

AB This invention discloses the prepn. of novel analogs of camptothecin {I; R, R1 = H, alkyl, alkenyl, alkynyl, alkoxy, halo, aryl, arylalkyl, arylalkenyl, arylalkynyl, -X1-(alkylene, alkenylene, alkynylene)-SiR12R13R14 (R12 = R13 = R14 = H, alkyl), -X1-(alkylene, alkenylene, alkynylene, phenylene, benzylene)-NR9R10 (R9, R10 = H, alkyl or nitrogen protecting group), OR6 (R6 = H, alkyl or oxygen protecting group); R2 = R3 = R4 = R5 = H, alkyl, alkenyl, alkynyl, alkoxy, halo, aryl, arylalkyl, arylalkenyl, arylalkynyl, amino, protected amino, nitro, -X2-(alkylene, alkenylene, alkynylene)-SiR12R13R14, -X2-(alkylene, alkenylene, alkynylene, phenylene, benzylene)-NR9R10 [X1, X2 = individually S, NR15(R15 = H, alkyl, N-protecting group or absent)], or OR8 [R8 = H, alkyl or -(alkylene, alkenylene or alkynylene)-SiR12R13R14]; R7 = H, alkyl, aryl, -SiR12R13R14 or absent when R11 = H; R11 = H, CO, SO2, CS, SO, alkylene, O or S; X = CH2 or absent} or a pharmaceutically acceptable salt thereof. Thus, I (R = R2 = R3 = R4 = R5 = R7 = H, R1 = CH2CH2Si(Me)3, R11 = O, X = CH2) (II) was prepd. by the reaction of homocamptothecin I [R = R1 = R2 = R3 = R4 = R5 = R7 = H, R11 = O, X = CH2(III)] with 3-trimethylsilyl-propanal.

AN 2000:790315 CAPLUS

DN 133:350387

TI Synthesis of novel highly lipophilic camptothecin analogs for use in treating cancers and leukemia

IN Kochat, Harry; Chen, Xinghai; Huang, Qiuli; Peddaiaghari, Seetharamulu; Hausheer, Frederick H.

PA Bionumerik Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000066127	A1	20001109	WO 2000-US12318	20000504

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-132414 P 19990504

OS MARPAT 133:350387

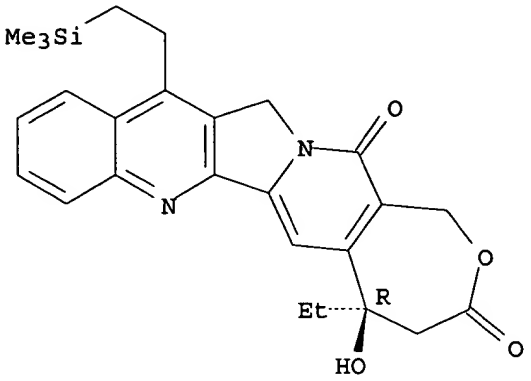
IT **289653-95-8P**, 7-Trimethylsilylethyl homocamptothecin
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Synthesis of novel highly lipophilic camptothecin analogs for use in treating cancers and leukemia)

RN 289653-95-8 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4

RE

(1) Bionumerik Pharmaceuticals Inc; WO 9807727 A1 1998 CAPLUS

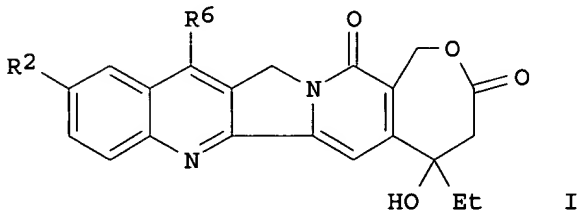
(2) Bionumerik Pharmaceuticals Inc; WO 9835940 A1 1998 CAPLUS

(3) Haridas; US 6057303 A 2000 CAPLUS

(4) Hausheer; US 5910491 A 2999 CAPLUS

L8 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2001 ACS

GI



I

AB Camptothecin analogs, such as I [R2 = H, OH, NH2, acyl, alkoxy, acyloxy, etc.; R6 = silyl, silylalkyl, silylalkenyl, silylalkynyl, etc.], were prepd. for use as antitumor agents. Thus, (.+-.)-10-amino-7-(tert-butyldimethylsilyl)homocamptothecin, a.k.a. DB 90, was prepd. via a multistep synthetic sequence starting from 4-ethyl-8-methoxy-6-(trimethylsilyl)-1H-pyrano[3,4-c]pyridine, tert-Bu bromoacetate, 1-bromo-3-tert-butyldimethylsilyl-2-propyne, and 4-(tert-Butyloxycabonylamino)phenylisocyanate. The prepd. homocamptothecins were tested for activity against MDA-MB-435 tumorigenic metastatic human breast cancer cells.

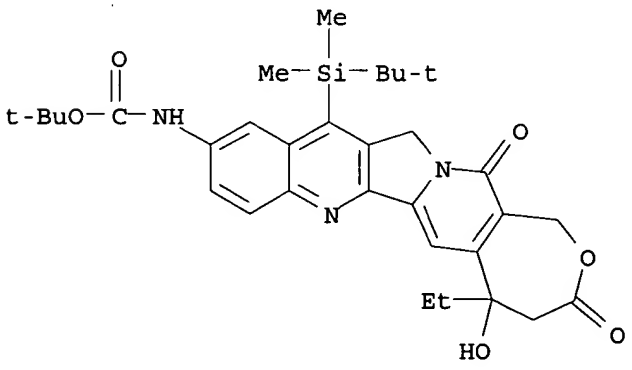
AN 2000:741925 CAPLUS

DN 133:296587

TI Preparation of camptothecin analogs for pharmaceutical use in the treatment of cancer
IN Curran, Dennis P.; Bom, David; Burke, Thomas G.
PA University of Pittsburgh, USA; University of Kentucky Research Foundation
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

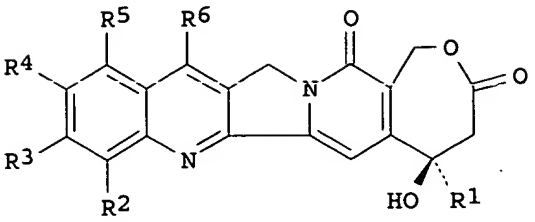
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061146	A1	20001019	WO 2000-US9401	20000407
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6207832	B1	20010327	US 1999-290019	19990409
US 2001003779	A1	20010614	US 2000-728031	20001130
PRAI US 1999-290019	A	19990409		

OS MARPAT 133:296587
IT **300582-81-4P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs for pharmaceutical use in the treatment of cancer)
RN 300582-81-4 CAPLUS
CN Carbamic acid, [12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RE.CNT 2
RE
(1) Bigg; US 5981542 A 1999 CAPLUS
(2) Bom; J Med Chem 1999, V42(16), P3018 CAPLUS

L8 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2001 ACS
GI



I

AB Camptothecin analogs I [R1 = alkyl; R2-5 = H, halogen, sulfonyloxy; R6 = H, Ph, alkyl, hydroxyalkyl, cycloalkyl, substituted alkyl, aryl, etc.] with topoisomerase inhibiting activity were prepd. for use as antitumor agents. Thus, I (R1 = Et, R5 = F, R2 = R3 = R4 = R6 = H) was prepd. by a multistep synthetic sequence starting from .beta.-ethyl-.beta.-hydroxy-2-methoxy-3-[(phenylmethoxy)methyl]-4-pyridinepropanoic acid 1,1-dimethylethyl ester, 2-amino-6-fluorobenzoic acid, and Et malonyl chloride. The prepd. camptothecin analogs were tested for inhibition of cell proliferation of HT29 human colon adenocarcinoma cells.

AN 2000:608751 CAPLUS

DN 133:193314

TI Preparation of optically pure camptothecin analogs for pharmaceutical use as anticancer agents

IN Lavergne, Olivier; Bigg, Dennis; Lanco, Christophe; Rolland, Alain

PA Societe de Conseils de Recherches et d'applications Scientifiques (S.C.R.A.S, Fr.

SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000050427	A1	20000831	WO 2000-FR461	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2790261	A1	20000901	FR 1999-2398	19990226
PRAI FR 1999-2398	A	19990226		

OS MARPAT 133:193314

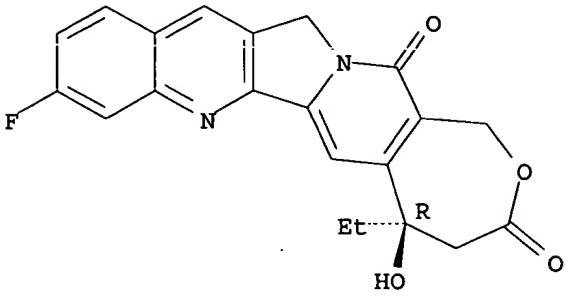
IT **284684-29-3P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of optically pure camptothecin analogs for pharmaceutical use as anticancer agents)

RN 284684-29-3 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

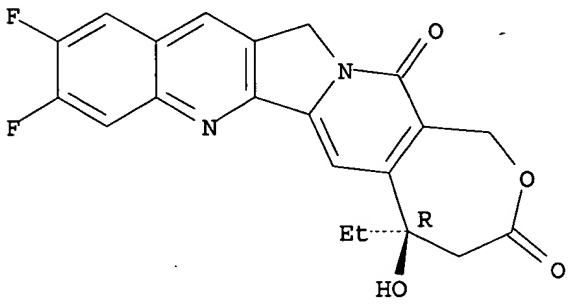


RE.CNT 9
RE
(1) Cazaux, J; WO 9911646 A 1999 CAPLUS
(2) Ejima, A; CHEMICAL AND PHARMACEUTICAL BULLETIN 1992, V40(3), P683 CAPLUS
(3) Lavergne, O; BIOORG MED CHEM LETTERS 1997, V7(17), P2235 CAPLUS
(4) Liberatore Anne Marie; WO 9828304 A 1998 CAPLUS
(5) Murali, D; WO 9835940 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB A review with 23 refs. Biomeasure and Institut Henri Beaufour, subsidiaries of Beaufour-Ipsen, are developing a series of homocamptothecin topoisomerase I inhibitors, which include BN-80915 and BN-80927, for the potential treatment of cancer. Phase I clin. trials of the lead compd., BN-80915, were initiated in Jan. 1999. Phase II studies are predicted to commence by the end of 2000. In June 2000, it was confirmed that BN-80245, the prototype compd. in this series, is not in (pre)clin. development and is being used as a research tool. BN-80915 was the lead compd. by 1998. BN-80915 is a difluorinated E-ring-modified camptothecin, with a 7-membered .beta.-hydroxylactone ring instead of the 6-membered .alpha.-hydroxylactone of classical camptothecin derivs.; it displays high toxicity toward tumor cell lines, in vivo oral activity in a no. of human tumor xenograft models at low doses and improved plasma stability, compared to other homocamptothecins. BN-80927, another member of the series, disclosed in 1999, inhibits both topoisomerase I and II in DNA relaxation assays. Preclin. studies have shown that the compd. demonstrates activity in HT-29, SW480 and SW620 colorectal cancer models, the N87 gastric cancer model, the small-cell lung cancer NCI-H82 model and the non-small-cell lung cancer A459 and SKMES models, among others. The compd. has been shown to be much more efficient at stimulating DNA cleavage by topoisomerase I than topotecan or SN-38. In vitro studies to investigate the induction of apoptosis in human myelocytic leukemia cells showed that the decrease of the mitochondrial transmembrane potential and the intracellular pH is more pronounced with BN-80915 than with topotecan or camptothecin, which may provide insight into the mechanism of action of the compd.
AN 2000:587727 CAPLUS
DN 134:36562
TI BN-80915, Beaufour-Ipsen
AU Osheroff, Neil
CS Department of Biochemistry, Vanderbilt University School of Medicine,

Nashville, TN, 37232-0146, USA
SO Curr. Opin. Oncol., Endocr. Metab. Invest. Drugs (2000), 2(3), 320-323
CODEN: COODF2; ISSN: 1464-8466
PB PharmaPress Ltd.
DT Journal; General Review
LA English
IT **220997-97-7P**, BN 80915
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antitumor pharmacol. of BN-80915 and BN 80927)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



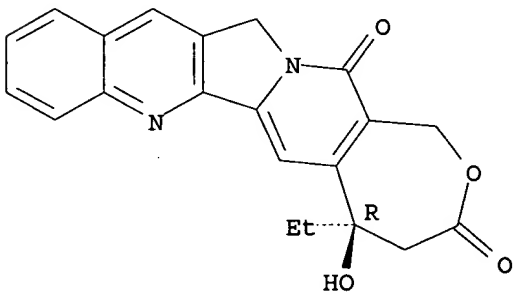
RE.CNT 23
RE
(5) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(16) Lavelle, F; Exp Opin Invest Drugs 1999, V8(6), P903 CAPLUS
(17) Lavergne, O; Bioorg Med Chem Lett 1997, V7(17), P2235 CAPLUS
(18) Lavergne, O; Bioorg Med Chem Lett 1999, V9(17), P2599 CAPLUS
(20) Lavergne, O; J Med Chem 1998, V41(27), P5410 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB Topoisomerase I (Topo I) is overexpressed in cancer colon tissues compared with normal colon tissues. Several anti-Topo I inhibitors are already successfully used in the clinic. We illustrate here the antiproliferative activity of a new class of Topo I inhibitors, i.e., E-ring-modified camptothecins with enhanced lactone stability. Forty-three human colon cancers were obtained from surgical resection and maintained under organotypical culture conditions for 48 h. Cell proliferation was assessed in these ex vivo tumor tissue cultures by tritiated thymidine autoradiog. As a validation of the methodol., we first analyzed in our model the antiproliferative activity of two clin. active topoisomerase II (Topo II) inhibitors, Adriamycin and etoposide, which are not active for colon cancers; and three Topo I inhibitors, camptothecin (CPT) and two clin. active compds. (esp. for colon cancers), i.e., topotecan and the active metabolite of irinothecan, SN-38. We then compared the antiproliferative activity of CPT, topotecan, and SN-38 against those of two investigational E-ring-modified camptothecins, i.e., BN80245 and BN80915. Three concns. (1, 10, and 100 nM) were studied for each compd.

The results indicate that the three Topo I inhibitors used as refs., i.e., CPT, irinothecan, and SN-38, were much more active than the two Topo II inhibitors, i.e., Adriamycin and etoposide, with SN-38 being the most efficient. The two investigational compds. BN80245 and BN80915 exerted higher antiproliferative activity than the three anti-Topo I ref. compds., with the highest activity obsd. for BN80915.

AN 2000:307978 CAPLUS
DN 133:202726
TI Homocamptothecin, an E-ring-modified camptothecin, exerts more potent antiproliferative activity than other topoisomerase I inhibitors in human colon cancers obtained from surgery and maintained in vitro under histotypical culture conditions
AU Philippart, Patrick; Harper, Luke; Chaboteaux, Carole; Decaestecker, Christine; Bronckart, Yves; Gordover, Laurence; Lesueur-Ginot, Laurence; Malonne, Hughes; Lavergne, Olivier; Bigg, Dennis C. H.; Da Costa, Pierre Mendes; Kiss, Robert
CS Departement de Chirurgie, Centre Hospitalier Universitaire Brugmann, Brussels, 1090, Belg.
SO Clin. Cancer Res. (2000), 6(4), 1557-1562
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
IT **186669-19-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative activity of Topo I inhibitors in human colon cancer)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



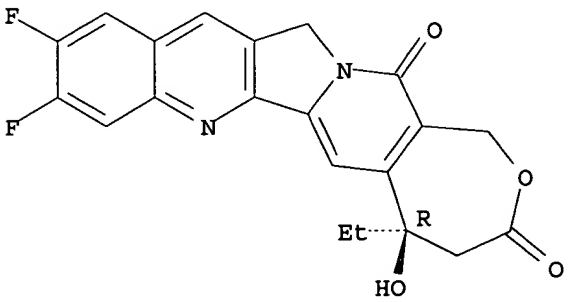
RE.CNT 18
RE
(1) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(2) Camby, I; J Natl Cancer Inst 1996, V88, P594 CAPLUS
(3) Cersosimo, R; Ann Pharmacother 1998, V32, P1334 CAPLUS
(5) Giovanella, B; Science (Washington DC) 1989, V246, P1046 CAPLUS
(6) Janssen, T; Prostate 1997, V30, P47 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB Homocamptothecin (hCPT) is an E-ring modified camptothecin (CPT) analog bearing a methylene spacer between the alc. and carboxyl functions of the CPT lactone. Combining pronounced inhibitory activity of topoisomerase I

(Topo I) with enhanced plasma stability, hCPT constitutes an attractive template for the elaboration of new anticancer agents. Fluorinated hCPT analogs, prepd. in enantiomerically pure form, were assayed by their stimulation of Topo I-mediated DNA cleavage. Translation into cytotoxicity against tumor cells was evaluated on HT29 human colon adenocarcinoma and on the multidrug resistant lung and bladder tumor cell lines, A549 and T24r. Good correlation is obsd. between the ability of the drugs to stimulate Topo I-mediated DNA cleavage and the resp. 50% inhibitory concns. (IC50 values) of the HT29, A549, and T24r cell growth. Fluorine substitution in the A-ring of hCPT was found to have a pronounced influence on biol. activity, providing several compds. which are .ltoreq.100-fold more potent than CPT in terms of IC50. Among these, 10,11-difluoro-hCPT has been selected for further development.

AN 2000:301517 CAPLUS
DN 133:114585
TI Topoisomerase I-Mediated Antiproliferative Activity of Enantiomerically Pure Fluorinated Homocamptothecins
AU Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Le Breton, Christine; Manginot, Eric; Cazaux, Jean-Bernard; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO J. Med. Chem. (2000), 43(11), 2285-2289
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **220997-97-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(topoisomerase I-mediated antiproliferative activity against tumor cells of enantiomerically pure fluorinated homocamptothecins in relation to DNA cleavage and pharmacokinetics)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

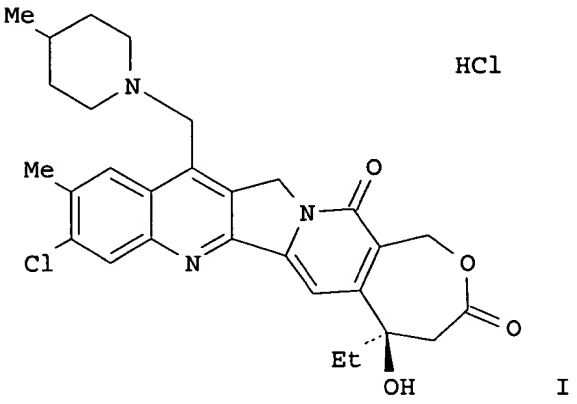
Absolute stereochemistry. Rotation (+).



RE.CNT 21
RE
(2) Bailly, C; Biochemistry 1999, V38, P15556 CAPLUS
(3) Bedeschi, A; Bioorg Med Chem Lett 1996, V6, P671 CAPLUS
(4) Burke, T; Ann NY Acad Sci 1996, V803, P29 CAPLUS

(5) Comins, D; J Am Chem Soc 1992, V114, P10971 CAPLUS
(6) Hsiang, Y; Cancer Res 1989, V49, P4385 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

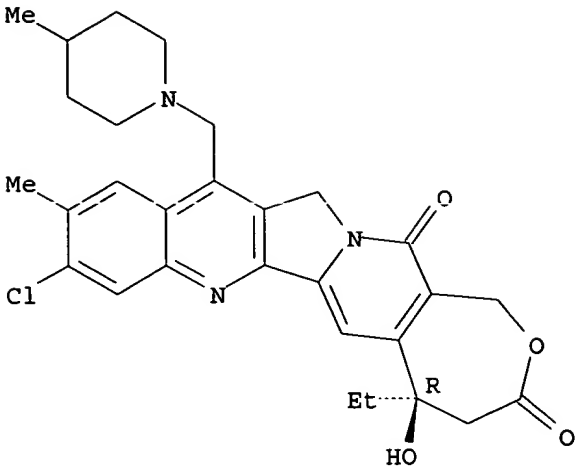
L8 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2001 ACS
GI



I

AB BN 80927 (I), a novel homocamptothecin deriv., inhibits both topoisomerase I and topoisomerase II mediated DNA relaxation and shows pronounced cytotoxicity against HT29, SKOV-3, DU145 and MCF7 human tumor cell lines.
AN 1999:614150 CAPLUS
DN 131:351522
TI BN 80927: a novel homocamptothecin with inhibitory activities on both topoisomerase I and topoisomerase II
AU Lavergne, Olivier; Harnett, Jeremiah; Rolland, Alain; Lanco, Christophe; Lesueur-Ginot, Laurence; Demarquay, Daniele; Huchet, Marion; Coulomb, Helene; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO Bioorg. Med. Chem. Lett. (1999), 9(17), 2599-2602
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
IT **220997-99-9P**, BN 80927
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and inhibitory activities of homocamptothecin BN 80927 on both topoisomerase I and II)
RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

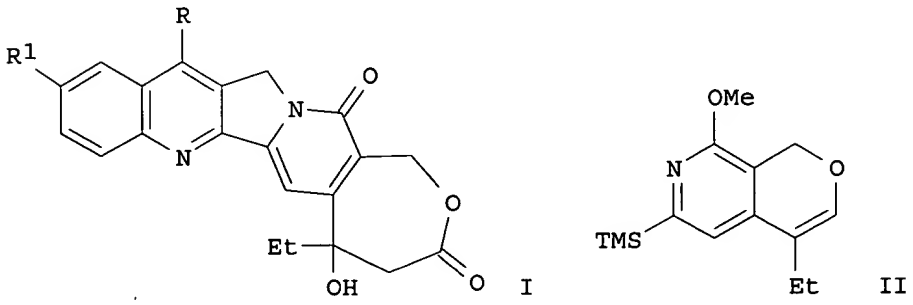
Absolute stereochemistry.



● HCl

RE.CNT 23
RE
(2) Bastow, K; Bioorg Med Chem 1997, V5, P1481 CAPLUS
(4) Cao, Z; J Med Chem 1998, V41, P31 CAPLUS
(5) Colbern, G; Clin Cancer Res 1998, V4, P3077 CAPLUS
(6) Comins, D; J Am Chem Soc 1992, V114, P10971 CAPLUS
(7) Comins, D; Tetrahedron Lett 1994, V35, P2819 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

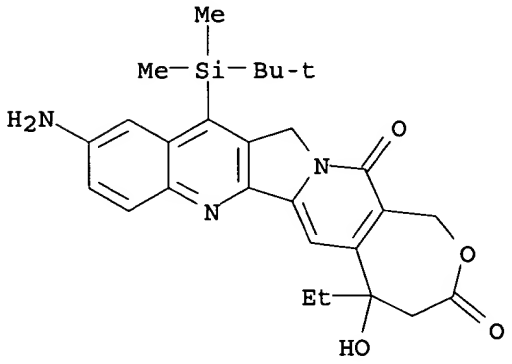
L8 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2001 ACS
GI



I II

AB The camptothecins I (R = Me3CSiMe2, Me3Si; R1 = NH2, OH, H) were prepd. starting from enol ether II. A variety of anal. and biophys. methods were employed to compare the blood component interactions and blood stabilities of I with camptothecin. I are potent topoisomerase I inhibitors that are stable not only in the mouse blood but human blood.
AN 1999:455126 CAPLUS
DN 131:299588
TI Novel A,B,E-Ring-Modified Camptothecins Displaying High Lipophilicity and Markedly Improved Human Blood Stabilities

AU Bom, David; Curran, Dennis P.; Chavan, Ashok J.; Kruszewski, Stefan; Zimmer, Stephen G.; Fraley, Kimberly A.; Burke, Thomas G.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO J. Med. Chem. (1999), 42(16), 3018-3022
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 131:299588
IT **247043-96-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(novel A,B,E-ring-modified camptothecins displaying high lipophilicity and markedly improved human blood stabilities)
RN 247043-96-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



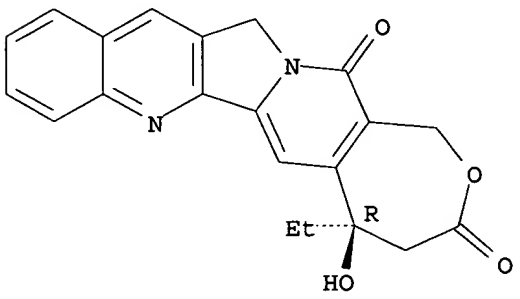
RE.CNT 22
RE
(1) Burke, T; Anal Biochem 1993, V212, P285 CAPLUS
(2) Burke, T; Biochemistry 1993, V32, P5352 CAPLUS
(3) Burke, T; J Am Chem Soc 1992, V114, P8318 CAPLUS
(4) Burke, T; J Med Chem 1994, V37, P40 CAPLUS
(5) Burke, T; J Pharm Sci 1995, V84, P518 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB Homocamptothecin (hCPT) is a semisynthetic analog of camptothecin (CPT) with a seven-membered .beta.-hydroxylactone resulting from the insertion of a methylene spacer between the alc. moiety and the carboxyl function of the naturally occurring six-membered .alpha.-hydroxylactone of CPT. This E-ring modification provides a less reactive lactone with enhanced stability and decreased protein binding in human plasma. Biol. testing against CPT revealed that, instead of being detrimental, the modified lactone of hCPT has a pos. impact on topoisomerase I (Topo I) poisoning properties. In vitro tests showed hCPT to fully conserve the ability to stabilize Topo I-DNA cleavage complexes and to stimulate a higher level of DNA cleavage than CPT. A similar trend toward improvement was also obsd. in antiproliferative assays with human tumor cell lines (including cells overexpressing P-glycoprotein). In two distinct in vivo models, using

L1210 murine leukemia or human colon carcinoma HT29, hCPT was found to be more efficacious than CPT. The slow, but irreversible, hydrolysis of hCPT, instead of the fast equil. of CPT, may account for its good in vivo activity. Overall, these results provide evidence that a highly reactive lactone is not a requisite for the Topo I-mediated antitumor activity of CPT analogs, and that hCPT is an interesting pharmacol. tool with improved soln. behavior as well as a promising new template for the prepn. of more efficacious Topo I poisons.

AN 1999:408033 CAPLUS
DN 131:193738
TI Homocamptothecin, an E-ring modified camptothecin with enhanced lactone stability, retains topoisomerase I-targeted activity and antitumor properties
AU Lesueur-Ginot, Laurence; Demarquay, Daniele; Kiss, Robert; Kasprzyk, Philip G.; Dassonneville, Laurent; Bailly, Christian; Camara, Jose; Lavergne, Olivier; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO Cancer Res. (1999), 59(12), 2939-2943
CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
IT **186669-19-2**, E-Homocamptothecine
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecin, E-ring modified camptothecin with enhanced lactone stability, retains topoisomerase I-targeted activity and antitumor properties)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 18
RE
(1) Burke, T; Ann NY Acad Sci 1996, V803, P29 CAPLUS
(2) Burke, T; J Pharm Sci 1994, V83, P967 CAPLUS
(4) Burke, T; J Pharm Sci 1995, V84, P518 CAPLUS
(5) Cao, Z; J Med Chem 1998, V41, P31 CAPLUS
(6) Chen, A; Cancer Res 1991, V51, P6039 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2001 ACS
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The camptothecin analogs (+)-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione (I) and (+)-1-[9-chloro-5-ethyl-5-hydroxy-10-methyl-3,15-dioxo-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoline-12-ylmethyl]-4-methylhexahydropyridinium chloride (II) were prepd. as antitumoral, antiviral or antiparasitic medicines. The invention also concerns a novel synthesis of intermediates of the products. Thus, (+)-5-ethyl-5-hydroxy-1,3,4,5,8,9-hexahydrooxepino[3,4-c]pyridin-3,9-dione (III), prepd. in three steps form tert-Bu 3-(3-benzyloxymethyl-2-methoxy-4-pyridyl)-3-hydroxypentanoate, was treated with 2-chloro-6,7-difluoro-3-quinolinylmethanol followed by cyclization to give I. I inhibited 50% proliferation of SW620 cells at 5.10-9 M.

AN 1999:184257 CAPLUS

DN 130:223476

TI Preparation of optically pure camptothecin analogs and their intermediates

IN Cazaux, Jean-Bernard; Lavergne, Olivier; Le Breton, Christine; Manginot, Eric; Bigg, Dennis

PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.

SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911646	A1	19990311	WO 1998-FR1768	19980807
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2768431	A1	19990319	FR 1997-10785	19970829
	FR 2768431	B1	20000324		
	AU 9889896	A1	19990322	AU 1998-89896	19980807
	EP 1007527	A1	20000614	EP 1998-941567	19980807
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9811405	A	20000829	BR 1998-11405	19980807
	JP 2001514261	T2	20010911	JP 2000-508685	19980807
	ZA 9807445	A	19990217	ZA 1998-7445	19980818
	TW 419479	B	20010121	TW 1998-87113646	19980819
	NO 2000000995	A	20000228	NO 2000-995	20000228
PRAI	FR 1997-10785	A	19970829		
	WO 1998-FR1768	W	19980807		

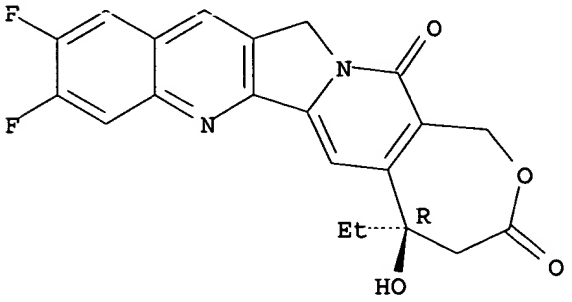
OS MARPAT 130:223476

IT **220997-97-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of optically pure camptothecin analogs)

RN 220997-97-7 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

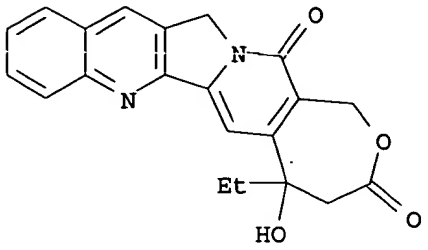
Absolute stereochemistry. Rotation (+).



RE.CNT 2
RE
(1) Comins, D; US 5459269 A 1995 CAPLUS
(2) Sod Conseils Rech Applic; WO 9700876 A 1997 CAPLUS

L8 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB Homocamptothecin (hCPT), a camptothecin (CPT) analog with a seven membered .beta.-hydroxylactone which combines enhanced plasma stability and potent topoisomerase I (Topo I)-mediated activity, is an attractive template for the elaboration of new anticancer agents. Like CPT, hCPT carries an asym. tertiary alc. and displays stereoselective inhibition of Topo I. The prepn. and biol. screening of racemic hCPT analogs are described. The 10 hCPTs tested were better Topo I inhibitors than CPT. Fluorinated hCPTs were found to have potent cytotoxic activity on A427 and PC-3 tumor cell lines. Their cytotoxicity remained high on the K562adr and MCF7mdr cell lines, which overexpress a functionally active P-glycoprotein. Fluorinated hCPTs were more efficacious in vivo than CPT on HT-29 xenografts. In this model, a tumor growth delay of 25 days was reached with 9,10-difluoro-hCPT at a daily dose of 0.32 mg/kg, compared to 4 days with CPT at 0.625 mg/kg. Thus difluorinated hCPT warrants further investigation as a novel Topo I inhibitor with high cytotoxicity toward tumor cells and promising in vivo efficacy.
AN 1998:772004 CAPLUS
DN 130:125250
TI Homocamptothecins: Synthesis and Antitumor Activity of Novel E-Ring-Modified Camptothecin Analogs
AU Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; Demarquay, Daniele; Prevost, Gregoire; Ulibarri, Gerard; Rolland, Alain; Schiano-Liberatore, Anne-Marie; Harnett, Jeremiah; Pons, Dominique; Camara, Jose; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO J. Med. Chem. (1998), 41(27), 5410-5419
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **186668-40-6P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of homocamptothecin analogs)

RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 49
RE
(1) Burke, T; Ann N Y Acad Sci 1996, V803, P29 CAPLUS
(3) Cao, Z; J Med Chem 1998, V41, P31 CAPLUS
(4) Carlson, B; Cancer Res 1996, V56, P2973 CAPLUS
(5) Ciufolini, M; Tetrahedron 1997, V53, P11049 CAPLUS
(6) Comins, D; J Am Chem Soc 1992, V114, P10971 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2001 ACS
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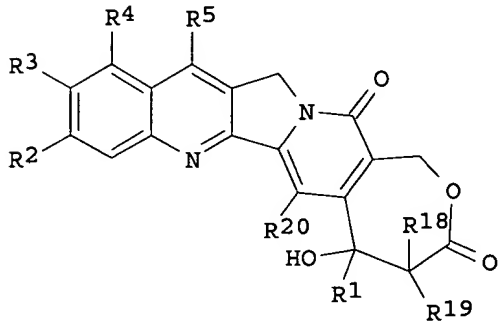

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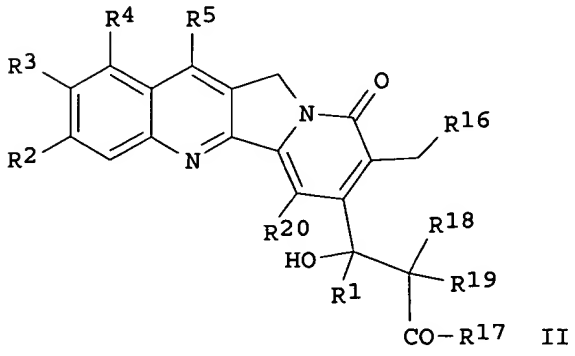


II

AB Title compds. I and II [R1 = alkyl, alkenyl, alkynyl, etc.; R2, R3, R4 = H, halo, haloalkyl, alkyl, alkenyl, cyano, etc.; R5 = H, halo, haloalkyl, alkyl, alkoxy, alkoxyalkyl, etc.; R16 = H, OH, acyloxy; R17 = OR6, NR6R7; R6, R7 = H, alkyl, hydroxyalkyl, alkylaminoalkyl, etc.; R18, R19 = H, halo, alkyl, alkoxy, OH; R20 = H, halo] are prepd. Thus, 8-formyloxymethyl-7-propionylindolizino[1,2-b]quinolin-9(11)-one, obtained in 2 steps via NaBH4 redn. of (S)-(+)-camptothecin and subsequent oxidative ring cleavage, reacted with tert-Bu bromoacetate in Et2O and THF contg. Zn and chlorotrimethylsilane to give the title compd. tert-Bu .beta.-ethyl-.beta.-hydroxy-.gamma.-(8-hydroxymethyl-9-oxo-11H-indolizino[1,2-b]quinolin-7-yl)propionate. In an in vitro study, 5-ethyl-4,5-dihydro-5-hydroxy-1H-oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(4H,13H)-dione (also prepd.) at 10 .mu.M effected ca. 58% redn. in the proliferation of L1210.

AN 1998:550712 CAPLUS

DN 129:136346

TI Preparation of camptothecin analogs as antitumors, antivirals, and parasiticides

IN Bigg, Dennis; Lavergne, Olivier; Pla Rodas, Francesc; Pommier, Jacques; Ulibarri, Gerard

PA Societe de Conseils de Recherches et d'Applications Scientifiques SCRAS S. A, Fr.

SO Fr. Demande, 88 pp.
CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

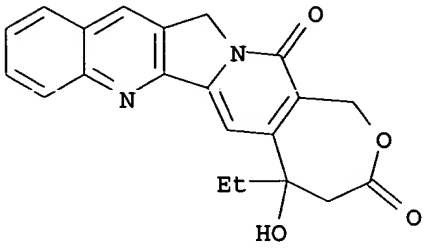
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2757514	A1	19980626	FR 1996-15774	19961220
	FR 2757514	B1	19990212		
	WO 9828305	A1	19980702	WO 1997-FR2218	19971205
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9853265	A1	19980717	AU 1998-53265	19971205
	AU 734485	B2	20010614		
	EP 946567	A1	19991006	EP 1997-950236	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9714170	A	20000229	BR 1997-14170	19971205
	JP 2001505922	T2	20010508	JP 1998-528448	19971205
	ZA 9711129	A	19990503	ZA 1997-11129	19971210
	NO 9902998	A	19990818	NO 1999-2998	19990618
PRAI	FR 1996-15774	A	19961220		
	WO 1997-FR2218	W	19971205		

OS MARPAT 129:136346

IT **186668-40-6P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as antitumors, antivirals, and parasiticides)

RN 186668-40-6 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



L8 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2001 ACS
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Camptothecin analogs I [R1 = alkyl, alkenyl, alkynyl, haloalkyl, etc.; R2 = R3 = R4 = R5 = H, CN, NO2, NHNH2, N3, halo, cyanoalkyl, nitroalkyl, etc.; R16 = H, acyloxy; R17 = alkoxy, amino, etc.; R18 = R19 = H, OH, halo, alkyl, alkoxy; R20 = H, halo; R21 = H, acyl, etc.; R16R17 = bond] were prepd. and formulated as prodrugs for use as antitumor, antiviral, and parasiticidal agents. Thus, camptothecin analog II.HCl was prepd. starting from 2-chloro-4-propionylpyridine, N-(tert-butyloxycarbonyl)glycine, and 3,4-difloroacetanilide via formation of intermediate alc. III and lactone IV, subsequent condensation of the alc. III with the amide moiety of IV, and intramol. cyclocondensation of the resulting chloride. The prepd. compds. were tested for topoisomerase inhibitory activity.

AN 1998:479535 CAPLUS

DN 129:109247

TI Preparation and formulation of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents

IN Bigg, Dennis; Lavergne, Olivier; Harnett, Jerry; Rolland, Alain; Liberatore, Anne-Marie; Lanco, Christophe; et al.

PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.

SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9828304	A1	19980702	WO 1997-FR2217	19971205

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

	GN, ML, MR, NE, SN, TD, TG				
	FR 2757515	A1	19980626	FR 1996-15775	19961220
	FR 2757515	B1	20000505		
	AU 9853264	A1	19980717	AU 1998-53264	19971205
	AU 734512	B2	20010614		
	EP 946566	A1	19991006	EP 1997-950235	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9713977	A	20000411	BR 1997-13977	19971205
	JP 2001506270	T2	20010515	JP 1998-528447	19971205
	NO 9902997	A	19990818	NO 1999-2997	19990618
PRAI	FR 1996-15775	A	19961220		
	FR 1996-15945	A	19961224		
	WO 1997-FR2217	W	19971205		

OS MARPAT 129:109247

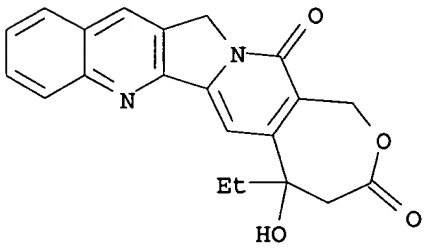
IT **186668-40-6P**

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and formulation of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents)

RN 186668-40-6 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



L8 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2001 ACS

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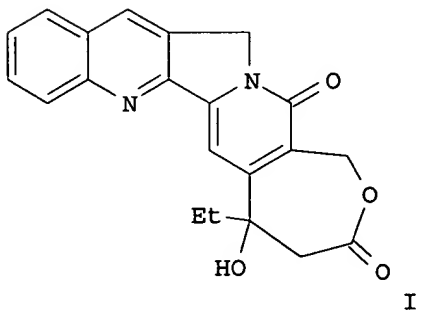
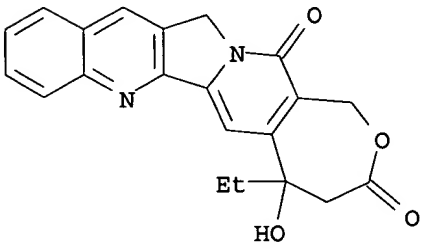


I

AB The crucial E-ring of camptothecin was modified to afford the homologous

.beta.-hydroxylactone deriv. BN 80245 (I). This compd., which is more stable than camptothecin, remains a potent inhibitor of both cell growth and topoisomerase I.

AN 1997:633920 CAPLUS
DN 127:331621
TI BN 80245: an E-ring modified camptothecin with potent antiproliferative and topoisomerase I inhibitory activities
AU Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Bigg, Dennis C. H.
CS Inst. Henri Beaufour, Les Ulis, F-91966, Fr.
SO Bioorg. Med. Chem. Lett. (1997), 7(17), 2235-2238
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
IT **186668-40-6P**, BN 80245
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of BN 80245, an E-ring modified camptothecin, with potent antiproliferative and topoisomerase I inhibitory activities)
RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



L8 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2001 ACS
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

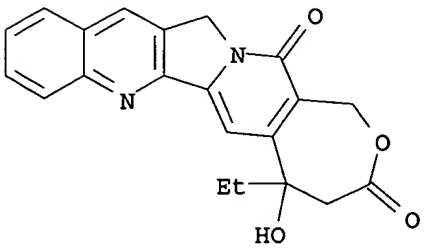
AB A camptothecin analogs I and II (R1 = alkyl, alkenyl, alkynyl, alkoxy, alkylthio; R2, R3, R4 R5 = independently, H, halo, alkyl, cyano, azido, hydrazino, heterocyclic substituted alkyl or acyl; R16 = H, alkoxy; R17 = alkoxy, amino, heterocyclic amino; R18, R19 = independently, H, halo, OH, alkyl, alkoxy; R20 = H, halo) were prepd. by a variety of synthetic paths and were tested for topoisomerase I inhibiting activity as antitumor agents. Thus, camptothecin analog III was prepd. form 7-ethylcamptothecin and reduced topoisomerase I activity to 96.9% at 10 .mu.M and 20.4% at 500 .mu.M of control activity levels. Camptothecin analog III was also tested against various tumor cell lines such as L1210 and HCT15.

AN 1997:140288 CAPLUS
DN 126:144433
TI Preparation of novel camptothecin analogs as antitumor agents
IN Bigg, Dennis; Lavergne, Olivier; Pla, Rodas Francesc; Pommier, Jacques;

Ulibarri, Gerard
PA Societe De Conseils De Recherches Et D'application, Fr.; Bigg, Dennis; Lavergne, Olivier; Pla Rodas, Francesc; Pommier, Jacques; Ulibarri, Gerard
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9700876	A1	19970109	WO 1996-FR980	19960621
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	CA 2225528	AA	19970109	CA 1996-2225528	19960621
	AU 9664608	A1	19970122	AU 1996-64608	19960621
	AU 716377	B2	20000224		
	ZA 9605318	A	19970124	ZA 1996-5318	19960621
	EP 835258	A1	19980415	EP 1996-924010	19960621
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI				
	CN 1192740	A	19980909	CN 1996-196127	19960621
	BR 9608639	A	19990629	BR 1996-8639	19960621
	JP 11508249	T2	19990721	JP 1996-503644	19960621
	US 5981542	A	19991109	US 1997-973561	19971202
	NO 9705988	A	19980219	NO 1997-5988	19971219
	US 6313135	B1	20011106	US 1999-325913	19990604
PRAI	GB 1995-12670	A	19950621		
	US 1996-610476	A	19960304		
	WO 1996-FR980	W	19960621		
	US 1997-973561	A1	19971202		

OS MARPAT 126:144433
IT **186668-40-6P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



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